NARCOLEPSY AND HYPERSOMNIA

A clinical and polygraphic study.

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INTRODUCTION

Many times in the course of this study, I have asked myself why I choose to investigate hypersomnia! It is perhaps natural to inquire into the habits of what Sir Derick Dunlop described aptly as the 'golden eagles' of medicine, and certainly hypersomniacs are rare and puzzling people. But there are other motives. I remembered that the very first patient demonstrated to our group in a Physiology tutorial was a narcoleptic. Her symptoms were perplexing to me and the concept of sleep as a disorder, then sounded novel and unreal.

But on further reflection I have realized that there is one motive which underlies all the sleep research in which I have been involved. That is to apply what has been discovered about the physiological changes that go on in sleep in the normal subject, to the patient, whether he should suffer from a physical illness or a psychiatric disorder. This motive has necessitated much work on the effects of drugs used in medicine and psychiatry on the sleep of normal subjects, and many nights of vigil to examine phenomena of sleep such as sleep walking or night terrors. Very recently my research has centred on the secretion of endocrines during sleep in the normal, with a view to further comparison with the secretion of these endocrines in pathological conditions.

Hypersomnia states were interesting when, in association with Dr. Ian Oswald and others I was involved in experiments on the effects of essential amino acids on sleep in normal subjects (OSWALD, et al. 1965). It was logical to apply the same tests to narcoleptic subjects (EVANS and OSWALD, 1965) and these results led me to extend my studies and include hypersomnia disorders in general in my group of patients.

The work has been possible only with the help of a large number of colleagues. I am particularly grateful to the late Dr. J.B. Stanton who was instrumental in the referral of so many patients from the neurological clinic; also to Professor J.S. Simpson, who gave me very much encouragement and access to patients. Numerous psychiatric colleagues also assisted in the supply of patients and the investigations would never have taken place without the continued support of Professor G.M. Carstairs who has always done all that is possible to support the sleep laboratory in its research. The diurnal sleep studies were greatly assisted by the help of Sister Faulkner and her staff, and the project has always benefited from the help, encouragement and criticisms from my colleagues in sleep research.

I am grateful for the encouragement and instruction I have received from Dr. Ian Oswald particularly at the/

/the inception of this work. My sympathies are with Miss Christine Robb who has patiently transformed my writing into readable type.

I. What is Hypersomnia?

KLEITMAN (1963) states that hypersomnia can be defined as uncontrollable somnolence and pathologically deep and prolonged sleep, from which it is sometimes difficult to arouse the sleeper, or keep him awake for any length of time after he has been awakened. In contrast Kleitman defined coma as complete loss of consciousness from which it was not possible to arouse the patient by even the most powerful stimulus. But as there are obviously grades of coma it is at once apparent that these definitions are not exclusive, and Kleitman acknowledges that in practice there are gradations and oscillations between them.

Approaches from the opposite pole of defining normal sleep in relation to hypersomnia, face equally difficult problems. Surveys in recent years (McGHIE and RUSSELL, 1962; TUNE, 1968) found that substantial numbers of subjects slept for longer than the mean 7-8 hours. In fact 2% of McGhie's sample of 2,446 subjects regularly slept for over 10 hours. In my own clinical work with students and younger patients I am aware of individuals who with reasonable regularity expect to sleep ten or more hours a day. But this observation alone does not allow me to consider such a person as a hypersomniac, but only as an example of a person at the extreme end of the normal Gausian distribution curve of sleep duration (McGHIE, 1962).

Another approach to the problem is to consider hypersomnia in terms of complaints made by individuals or their friends and relatives, about excessive sleep.

Surveys show with reasonable consistency that sleep deteriorates particularly with increasing age, but also with 'nervousness' and various physical illnesses (McGHIE and RUSSELL, 1962; McGHIE, 1966). The increasing problem of insomnia is confirmed by the escalating demand for hypnotics and tranquillizers (Ministry of Health Report No: 110, 1964). The implication that doctors and patients alike consider sleep as a necessity which must be procured, raises the question why people should ever complain about hypersomnia.

On theoretical and practical grounds it would seem reasonable to complain of hypersomnia under a number of different conditions.

Complaints may arise if the subject became the object of amusement and derision because of his sleep. Extremely sleepy people may be seen as 'lazy' or be the object of amusement as was the fat boy 'Joe' in Dickens' Pickwick Papers. To be considered a 'sleeping beauty' or Rip Van Winkle or dormouse (La Dormeuse d'Oknö, Froderström, 1912) may be sufficient reason to seek medical help or at least medical confirmation of one's disability.

On the other hand, if the excessive sleep leaves the individual in a state of depressed activity or/

/or performance this may constitute a reason for complaint. Such a view was considered by ARETAEUS in the second century A.D. who stated "much sleep.....is bad as it tends to stupify the senses and the performance of every action is rendered dull and languid from a redundancy of vapour". (ADAMS, 1856).

On other grounds, if the excess of sleep is sufficiently gross so as to seriously interfere with daily functioning of the individual, this would be an adequate cause for complaint. Also if the sleep itself was accompanied by disturbing symptoms such as nightmares, respiratory difficulty, excessive hunger or obesity, complaint may be more likely.

Finally, as the suphistication of the public increases, hypersomnia may be seen as a symptom of serious disease such as cerebral tumour or diabetes and this concern may take the patient to the doctor.

But while it is possible to see such reasons in operation or at least consider them in theory, the ~~corollary~~ corollary is that there may be many people living in the community who suffer from a degree of hypersomnia which is so uneventful or insufficiently oppressive to make the individual consider himself or herself to be ill. So the dividing line between 'normal' sleep and hypersomnia is about as indefinite as is the division between hypersomnia and early coma, and a more sophisticated measure is needed/

/needed to distinguish between them.

In the past fifteen years much research has been directed towards a greater understanding of sleep. In particular, more is now known of the "internal structure" of normal sleep. Such fresh observations with their attendant theories and hypotheses prove a stimulus to research in allied fields, and may lead to a greater understanding of the pathological states.

It was logical therefore to investigate prospectively the sleep of patients who complained of hypersomnia as they reported for investigation at both psychiatric and neurological clinics in this region.

Commencing in 1965 I undertook to investigate the sleep of such subjects and institute any further investigation or treatment that seemed desirable.

The results of this study are submitted for the degree of Doctor of Medicine at the University of Edinburgh.

II. Clinical concepts of Hypersomnia, of lethargics and 'sleeping girls'.

Clinical views on the problem of hypersomnia have undergone many changes. At some points in time there have been great interest in this anomaly of sleep, but at others such problems have seemed trivial.

While the observations of Aretaeus on sleep disorders were extensive and often very definite, it was not until the Nineteenth Century that an extensive medical literature developed.

Aretaeus devoted two books to the problem of 'Lethargy' and described in detail a regime of dietary control coupled with exercise and gymnastics in the treatment of these conditions. "Lethargics are to be laid in the light and exposed to the rays of the sun (for the disease is gloom); and in a rather warm place for the cause is congelation of the innate heat" (ADAMS, 1856). His views remained in acceptance to some extent well into the nineteenth century.

In the seventeenth century there was the report of the case of Epimenides, the Cretan poet who retired to a cave and slept for fifty-seven years.

During the seventeenth and eighteenth century a number of isolated Masters' theses and public documents refer to the problem of hypersomnia. (HARTMAN, 1686; VAN NOORAT, 1706).

An excellent medical commentary of the seventeenth century on the problem of hypersomnia, occurred in 'De anima brutorium' by Thomas Willis, 1672. He made a plea that hypersomnia should be regarded as a disease entity, not 'an evil habit', differing from coma and lethargy. His clinical picture was of episodes of sleep which could be interrupted by 'friends or servants' when the hypersomniacs could 'remember many things and converse with their friends, though prove again to sleep'. The explanation of hypersomnia offered by Willis was a cycle of cerebral oedema → raised intracranial pressure → cerebral anaemia. Treatment with bleeding and purges was therefore appropriate, but interestingly Willis also advocated 'at eight of the clock in the morning and at five in the afternoon, let them drink a draught of coffee, or the liquor prepared from that berry, first boiling in it the leaves of the Sage or Rosemary till it has got a greenish tinge'.

PIZLER (1708) saw hypersomnia in terms of an obstructive and inhibitive block at the level of the cerebral peduncles. Van Kasthoven of Leyden reported a case of a peasant of Woëkwig who was alleged to have fallen asleep on June, 29th 1706, awakening on January, 11th 1707, only to fall asleep again until March, 15th 1707. (GOULD and PYLE, 1897).

A woodcut dating from approximately 1772 records the case of Marianne Olivarne of Saint-Marcel d'Ardeche in Vivarais.

She was stated to suffer from an annual episode of prolonged sleep of nineteen days' duration from March, 1st onwards. At this time she was aged fifty-five and reported this annual sleep started when she was eighteen years.

Gould and Pyle were able to gather together a total of eight similar cases of 'catalepsy, trance and lethargy' from the literature of the nineteenth century. Their cases were 'asleep' for periods of up to five years, but one report (GIMSON, 1863) was of a twelve hour duration sleep which was recurrent.

WADD (1810) reported a rather different problem of continued drowsiness rather than prolonged sleep. "A country tradesman aged about thirty, of a short stature.... and very fat applied to me for assistance. He complained of perpetual drowsiness and lethargy.....he could scarcely keep awake whilst he described his situation".

A prolonged sleep lasting eight days which started suddenly in a young woman was described by FOURNIER (1813), and perhaps the best known "sleeper" was described by Charles Dickens in the Posthumous Papers of the Pickwick Club; LONDON, 1837. Joe, Mr. Wardle's boy was recorded to sleep in remarkable situations, even between the times of knocking at the door and awaiting its opening. He was chronically soporofic and grossly obese, "a fat and red faced boy in a state of somnolency".

Over the next forty years a number of cases were recorded which fall into three broad groups.

1. There were patients who were recorded to sleep for prolonged periods at a time but were normal or even over-active between sleep periods. The most celebrated patient was 'Sleeping Effie', a Fife woman, who wandered for long walks around the countryside between periods of sleep lasting from one to five weeks. (EDWARDS, 1848). Cases of sleep lasting from 36 hours to several months were described by GIMSON, 1863; COUSINS, 1863; BLONDET, 1864; WYATT, 1865; MENDEL, 1872; GAIRDNER, 1878 and DOWNE, 1879.
2. Patients who reported long hours of sleep but not extending through a twenty-four period. (HANDFIELD JONES, 1870; correspondant "A.D." in Lancet, 1867; MORE MADDEN, 1881; LASEQUE, 1882; SAHLMANN, 1881; MATAS, 1884).
3. Patients who suffered several episodes of short lived or very short lived sleep during a day, with or without a sense of continued drowsiness. The first of these cases of short lived episodes of sleep were reported independantly by THRUMEN, 1841 and FRICKER, 1841.

GRAVES (1851) reported the case of a man of 'plethoric' habit who was chronically somnolent but had frequent 'attacks' of sleep which could last less than a minute. (This is the first example of the concept of an "attack" of sleep)/

/sleep). CAFFE (1862) similarly reported on a 'large and corpulent' man who had diurnal attacks of somnolence. Caffe considered that his patient suffered from chronic meningitis.

WESTPHAL (1877) described a case of a forty year old man who suffered several forms of attack. Under powerful excitement he lost his speech with great "trembling and weakness". In other attacks he would fall, "his jaw twitching, eyes half open and respiration hastened". At the end he had a bowel motion. In yet different attacks he became suddenly drowsy and would sleep even in the street until wakened accidentally.

FISCHER (1878) reported on the symptoms of a twenty-one year old woman who suffered two to six attacks of sudden sleep a day, each lasting from five to sixty minutes. They were accompanied by "much trembling". The patient's sister had similar symptoms at one time. In 1880, MENDEL and PORTER both reported independently on patients with short lived attacks of sleep lasting up to thirty minutes, although Mendel's patient had severe vaso-motor disturbances with the attack, and one of Porter's cases suffered from severe vertigo.

Marked physical symptoms in association with attacks of sleep were also reported in several cases prior to 1880.

PAZ (1876) reported on a 39 year old farmer who suffered severe neuralgic pains prior to the attacks of/

/of sleep. It was suspected that he suffered from syphilis.

Also SIEMENS (1879) observed a case in which both attacks of sleep and epileptic seizures occurred.

Of Narcolepsy

It was against this background of extended sleep; prolonged over-night sleep; sleep attacks with some evidence of physical disease in association, that GÉLINEAU (1880) reported his case in terms which have frequently been quoted. "I propose to give the name of narcolepsy (somnolence and to seize) to a rare neurosis, and one that is little known at the present time characterized by an imperious desire to sleep, sudden and of short duration, reproducing itself at intervals more or less closely related".

Gélineau's case, a cooper aged 38 had suffered a rather indefinite head injury but denied convulsions or epilepsy. He complained not only of sudden, short lived and demanding attacks of sleep but that in the presence of severe emotion his legs trembled and he stumbled. Attacks of weakness associated with emotion frequently led to sleep. Gélineau noted the case reported by Caffe in 1862 and considered this as further proof that the disorder existed.

In that he seemed unaware of the existing literature and that this literature was orientated towards the association of the attacks of sleep with some physical disease, Gélineau's claim to a 'rare neurosis, or one/

/one that is little known' seemed curiously ill founded. Westphal and Fischer considered their cases 'epileptoid' and Caffe had thought his patient suffered from meningitis.

The reaction to Gélineau's proposal was largely negative. In 1881 Workman reviewed his case and discussed it in relation to a case of his own who suffered from cerebellar ataxia - the similarity was the 'drunken' gait of Gélineau's patient when weak, and he called on Gelineau's evidence of bradycardia in his patient to suggest that cerebral anaemia was the cause of the somnolence.

Also, in 1882 BALLET described three cases in which short precipitant diurnal periods of sleep occurred which he believed was due to some circulating toxin.

There was a further school of thought in relation to sleep. The collection of 'hysterics' at the Salpetrière allowed much observation on episodes of prolonged sleep in this population (CHARCOT, 1882). Charcot and his colleagues were particularly valuable in that they emphasized the need to investigate the patient for other stigmata of hysteria such as anaesthesia before making the diagnosis.

GAY (1880) described a case of prolonged sleep in a girl who was aroused on two occasions by placing tartar emetic on her tongue. On the third occasion, mention of doing this as a test caused her to awaken and be discharged from hospital.

GAIRDENER (1883, 1884) gave a lengthy account of a 32 year old female who developed a prolonged 'trance' after childbirth and who was observed to snore during the night hours, but not in the daytime, 'a sleep within a sleep'. She roused after a visit from her husband. Gairdener also described in 1878 a girl whose episodes of somnolence alternated with violent choreic movements. A diagnosis of hysterical malingering was made.

A valiant attempt to draw these schools of thought together was made by DANA in 1884. He reviewed fifty cases of 'morbid somnolence' from the literature and included five of his own and two others from a colleague, Dr. Pulza of New York. Dana summarized others' views initially by concluding that drowsiness was a symptom of many physical diseases. His list included old age, cerebral vascular disorders, meningitis and other cerebral infections, toxaemias such as malaria, uraemia and syphilitis, diabetes, obesity, cerebral hyperaemia and anaemia, cerebral tumour and injury, exhausting illness and African sleeping sickness.

On a phenomenological basis he considered that patients might suffer from:-

a) a great prolongation of natural sleep
b) a recurrent tendency to brief periods of sleep without intervening drowsiness
c) a constant state of drowsiness "to which he yields on occasion"/

/occasion"

d) periodical attacks of somnolence and lethargy which may last days, weeks or months

e) repeated and single lethargic attacks of a milder nature - the 'sleeping or fasting girls' are an example.

The differences between groups D and E are not clear. However, Dana conceded that such a system did not entirely describe what was happening to patients.

On a pathological basis he described three processes.

1) The Epileptoid sleeping states. He saw these as equivalent to petit mal and grand mal attacks.

2) The Hysteroid sleeping states. These included lethargic and 'sleeping girl' cases as well as chronically soporific patients and patients with short lived attacks of sleep.

3) An idiopathic group, which he called a special morbid hypnosis. They could be organically based or simply be people whose need for sleep was abnormal.

Points of help in diagnosis were that hysteroid sleeping states occurred in a younger age group with a previous history of some nervous symptom. They were often precipitated by some severe emotion.

In his survey of case material, Dana included Gelineau's case as well as those of Westphal, Fischer and Caffe in the Epileptic group because of the 'trembling' features. His idiopathic group contained a number of cases where the/

/the possibility of some cerebral pathology was present and other cases which he could not fit into a Hysteric or Epileptic basis.

In another approach to the problem, FOOT (1886, 1887) after describing a case who suffered from attacks of sleep, emphasized the demanding quality of the sleep attack suggesting that the term Narcolepsy might be replaced by the term Hypnolepsy, as narcolepsy conveyed only the idea of ordinary sleep and there was a 'numbness or rigidity' about the sleep attack. The word 'vapkn' conveys no idea of rigidity or numbness but only that of ordinary sleep! Nevertheless Foot was adamant that this was not an epileptic condition.

CATON (1889) described a case of 'narcolepsy' to a meeting of the Clinical Society of London, with Christopher Heath, F.R.C.S. in the Chair. Caton's patient became remarkably stout in his thirtieth year and was troubled by constant drowsiness. In sleep he suffered a closure of the glottis which amounted to obstruction with resulting cyanosis. The condition was ascribed to a 'toxaemia'. The President reported a case of Dr. Guy's who slept so heavily that her husband was able to have intercourse with her while she was asleep; he further observed that many persons in Church suffered from a modified form of narcolepsy!

From the discussion of this paper it is obvious that the term narcolepsy had essentially no meaning at all at this time. It was used quite freely to describe any sleepy disorder - from cases of cerebral syphilis to drowsy people listening to a Church sermon.

This point was made very clearly by several later authors who felt that the organic basis for sleep disorders was being underestimated.

JACOBY (1893) described a case under the title of 'periodic sleep seizures of an epileptic nature'.

LEVI (1896) described somnolence and narcolepsy in the presence of hepatic disease, and MOYER (1898) whose description of a young man who suffered attacks of sleep and at one time had a number of precipitous attacks of loss of consciousness, was entitled 'a case of paroxysmal sleep, sleep epilepsy or narcolepsy'.

The general feeling in those who discussed Gélineau's concept of narcolepsy as a specific disorder was that it had some as yet undiscovered cerebral pathological basis.

WEIR MITCHELL (1890) had in a series of papers (1876, 1878) described many of the phenomena of sleep, and collected from the literature eighteen cases of prolonged sleep. Autopsy examination on the brain of one was unremarkable although some starch granules were noted in the ventricular system.

MacCARTHY (1900) was very doubtful of the diagnosis of narcolepsy in the cases he prescribed and took the view that there must be some cerebral lesions. He pointed out that at this time "Eickhorst was including narcolepsy or narkoepilepsia as an occurrance of epilepsy; Oppenheim as a symptom of hysteria and Lamacq denying the possibility of any such condition as hysteronarcokepsy or epileptic narcolepsy and attributing the condition to the derangement of function of some of the viscera".

At the beginning of the century narcolepsy was used as a term to describe a patient with sleep attacks where some undiscovered pathology was suspected.

FURET (1901) drew attention to the presence of somnolence in 'nutritive disorders', diabetes mellitus, infections, alcoholism and drug intoxications to suggest that narcolepsy was a state of autointoxication. He further suggested that epileptic attacks which he considered were another manifestation of autointoxication, were frequently synchronous with epilepsy. SAINTON (1901) put forward much the same view. This work was however challenged by the work of STERN (1902) who could find no evidence in his investigations of a patient with narcolepsy of any sign of intoxication. His finding of increased urinary chlorides was suggested as a factor in producing somnolence as the chloride was seen as a decisive force in osmotic pressure regulation. This finding was reminiscent of/

/of MARDUEL (1872) who reported a great increase in urea excretion in a case of somnolence.

A return to Gelineau's views was made by LOEWENFELD in 1902. He pointed out the significant of the attacks of weakness triggered by emotion which were present in Gelineau's case. Such attacks he termed KATAPLEKTISHE STARRE - an inability to maintain an erect posture, and he made Gelineau's syndrome one of a double symptomatology. This view was well received by German neurologists.

But there were two problems. One was that the term Catalepsy had long been in use in connection with states of prolonged sleep and trances and "KATAPLEKTISHE" was not sufficiently different. On the other hand there was reported at this time a syndrome of motor weakness produced by laughter - 'Lachschlag' of Oppenheim (1902). As Oppenheim reported some of his cases became unconscious with laughter, the relationship of Lackschlag: KATAPLEKTISHE: Epilepsy was confusing. Particularly as it was also known that some epileptics suffered from what came to be called 'drop attacks'.

A further difficulty was the work of FRIEDMANN (1906). He described a benign state in children of repeated attacks of altered consciousness - an 'absence' during which consciousness was not entirely lost and some automatic movements occurred. Friedmann was anxious to disassociate them from epilepsy because of their good prognosis. He called the absences 'short narcoleptic attacks' and/

/and stated emphatically that the attacks had nothing in common with normal sleep. Unfortunately his use of narcolepsy served to confuse the situation further and enhance the association between sleep attacks and epilepsy.

A careful attempt to revaluate the syndrome was made by CAMP (1907). He was well aware of the difficulty of the increasing number of physical causes that could produce somnolence, and the fact that Epileptics may complain of sleepiness. Camp definitely disagreed with Friedmann's use of the term narcolepsy for attacks which were obviously epileptic, but was emphatic that cases in which brief sleep attacks occurred could be differentiated from cases in which somnolence was a symptom of organic disease. "Why not make of these cases of narcolepsy a separate disease or at least a syndrome?" Camp described narcoleptics as individuals with a 'functional degeneration of the nervous system".

A further attempt to restore the situation was made by Sir William Gowers in his book 'The Borderland of Epilepsy' 1907. He proposed that the term narcolepsy should be reserved for 'cases in which definite sleep interrupts a normal state'. Further he suggested narcolepsy must not apply when a 'sleep state is interrupted only when the sufferer is aroused'. Here the old term 'somnosis' should be used. (Somnosis was a term originally employed by Nicolas to indicate African sleeping sickness).

But the general thesis that narcolepsy although not necessarily connected with epilepsy, was essentially an early andicator of organic or nervous disease - a degeneration symptom, was still present.

BLOGETT (1906) quoted the work and views of RAYMOND (1905) who believed that 'mental hebetude and abnormal slumberous conditions are often observed among the first indications of serious nervous or mental impairment'.

Blogett traced a variety of symptoms in five successive generations. Despite the difficulty of obtaining information he made a case that the paternal grandfather of his patient had suffered from venereal disease, and his various descendents suffered from blindness, bone diseases, idiocy, nervousness and narcolepsy.

During the next five years the role of narcolepsy was that of a suspect cerebral pathological condition confused with epilepsy.

There were however several studies of prolonged sleepers (PAUL, 1911). He reviewed reports by Farez, Carret and Berillon on cases of prolonged sleep. Their studies amply confirm the association of these conditions with hysteria, as other dissociative features were found. Fröderström completed this series with the famous case of La Dormeuse d'Oknö, 1912.

However the German school of neurologists followed/

/followed Loewenfeld's duality concepts and used the term narcolepsy only for three cases showing ~~catalepsy~~ cataplexy as well as sleep attacks. (HENNEBERG, 1916; REDLICH, 1915; STOKER, 1913; JOLLY, 1916).

SINGER (1917) advocated a return to the term 'Hypnolepsy' originally used by Foot in 1886 for precisely the opposite reason, i.e. to get away from the 'organic' concepts associated with the term narcolepsy and emphasize the attack as 'resembling natural sleep'.

But these attempts to limit the syndrome largely failed because almost all these authorities were forced to concede that there were many patients who suffered little or nothing in the way of cataplexy and yet seemed to belong to the narcolepsy group.

Two closely linked events provoked much discussion and writing about sleep and its disorders. The first World War provided much material on the effects of cerebral injury, and the successive episodes of encephalitis lethargica which swept over Europe after the War taught physicians a great deal about the effects of small isolated brain lesions.

Both SOUQUES (1918) and LHERMITTE (1918) were impressed by cases in which sleep attacks and cataplexy followed head injury whether localised or diffuse.

The gross changes in circadian sleep/arousal patterns seen in the encephalitic patients made a big impression and through the pathological studies of Von ECONOMO (1926)/

/1926) and others, the relevance of small localised lesions in the vicinity of the third ventricle particularly in the diencephalon to sleep disorders became very real. A sleep centre in this area had originally been postulated by MAUNTHER (1890). DERCHUM (1925) added to the evidence by describing a case of narcolepsy as a patient with pituitary disease.

Narcoleptic pictures which included classical cataplexy was reported in post encephalitics by REDLICH (1925), PERRIER, 1925 and SPILLER, 1926.

WENDEROWIC (1924) made an attempt to rationalize the situation. He objected to the term Narcolepsy as he considered its application was too great and he adopted FOOT and SINGERS' proposals to use Hypnolepsy as a generic term for the disorder.

He classified Hypnolepsy into:-

1. Genuine hypnolepsy (Gelineau's disease)
2. Symptomatic hypnolepsy (probably a post encephalitic syndrome)
3. Narcolepsy (symptomatic hypnoid states of previously known illnesses).

Genuine hypnolepsy was considered a rare disease and cataplexy was a necessary component of the syndrome.

Hypnolepsy never succeeded as a term, but a division between idiopathic or 'genuine' narcolepsy and symptomatic narcolepsy continued.

The necessity of including cataplexy in the syndrome of genuine narcolepsy was criticized by many authorities (GOLDFLAM, 1924, CRUSCHMANN and PRANGE, 1925, MATZDORFF, 1925). All found cases which conformed to Gelineau's syndrome except that cataplexy symptoms were insignificant or absent, and this led Matzdorf to propose that there were larval forms of the disease.

Against this background ADIE submitted his thesis for Doctor of Medicine at this university in 1926 entitled "Idiopathic Narcolepsy", a disease sui generis, with remarks on the mechanism of sleep. He stated 'one of my objects is to rescue the word narcolepsy from the confusion that now surrounds it, and to reinstate it as the name of a highly remarkable and by no means rare disease with peculiar and unmistakable features that distinguish it clearly from epilepsy and other morbid conditions in which excessive or untimely sleep is an occasional symptom'.

Adie based his findings on six of his own cases and fifteen other examples taken from the literature. He considered both sleep attacks and cataplexy 'curious attacks on emotion in which the muscles relax suddenly' were necessary for the diagnosis, but included three cases on his series in which cataplexy was absent. He differentiated narcoleptic attacks from petit mal as the former were frequently reactive, that is a response to emotion or other environmental factors. Adie (1924) had already/

/already discussed the benign children's disorder which FRIEDMANN (1906) called Narcolepsy and proposed it should be called Pyknolepsy and regarded as a very mild but recurrent form of juvenile epilepsy. He did acknowledge that the 'attack' quality of the sleep and of cataplexy was reminiscent of epilepsy but reminded his readers of the benign course of the narcoleptic disorder, its resistance to anti-convulsants and the rousability of the narcoleptic sleeper - emphasizing that it was after all only a normal sleep.

Hysteria, patients with lachschlag, pituitary disease, obesity, cerebral tumour and encephalitis, Adie suggested should be seen as conditions which could mimic the sleep attacks of the narcoleptic, but never the cataplectic attacks. ('An organic lesion caused symptoms that were usually due to a functional disorder at the same site').

Finally, Adie put forward the concept that the narcoleptic suffered from a process of 'internal inhibition' along the lines suggested by Pavolov (1923), a functional process which could be triggered by reflexes. This concept of inhibition he correlated with the current views of a sleep centre which Adie suggested existed at a thalamic level, although he discussed the evidence of a diencephalic centre. In his conclusion Adie stressed that the sleep attacks of the narcoleptic were of 'normal' sleep produced by a process of reversible inhibition at a sleep centre, or at a cortical level, rather than a lesion which could give rise to/

/to 'symptomatic' narcolepsy.

This view was strongly opposed by several authorities (LHERMITTE and TOURNAY, 1927; WILSON, 1928). Wilson reviewed the current ideas and reminded his readers that Hughlings Jackson's case for regarding epilepsy as a symptom not a disease, was equally true of narcolepsy. Thus, Wilson felt it was much more logical to speak of 'the Narcolepsies' as a group rather than to make artificial categories of 'genuine' or 'symptomatic' narcolepsy. ~~He saw~~ He saw all narcolepsy as 'symptomatic' but acknowledged that the pathological basis for some cases was not yet known.

The possible relationship with epilepsy Wilson regarded as 'not proven'. In the first place there was no completely exclusive definition of epilepsy which would serve to differentiate it from narcolepsy. On semantic grounds he pointed out that as narcolepsy and epilepsy were both merely symptoms of some underlying cerebral disorder, it was an impractical exercise to separate them, and he cited the known cases in which epilepsy and narcolepsy had been shown to co-exist. Wilson described how he had been able to record a positive Babinski response during cataplexy in one patient which he interpreted as evidence of cerebral dysfunction similar to epilepsy although he acknowledged that a positive response had been found during normal sleep. The increasing number of pathological processes which gave rise to sleep symptoms were seen by Wilson as further evidence/

/evidence that a greater understanding of the pathology underlying 'idiopathic' narcolepsy was imminent and he stated that 'the correct attitude in my opinion is to suspend judgement and to await further contributions to our knowledge'.

The problem of whether the 'sleep' attack was in fact 'normal' sleep concerned Wilson greatly and he pointed out the problem of the patients who could describe various events which occurred while they were apparently asleep.

Finally, Wilson emphasized that many of the complaints of the narcoleptic were only an exaggeration of normal experience - the sleepy attacks, the weakness on emotion, the feeling of paralysis and the hallucinations associated with the sleep, he pointed out were described by Weir Mitchell thirty years before in many normal people. Thus narcolepsy seemed to Wilson to be a syndrome founded on one rather indefinite symptom - sleep attacks - after which all cases had been moulded to fit the concepts of the 'disease'.

BROCH (1928) surveyed the developments of the decade and supported Adie's concept of narcolepsy as a reversible wave of inhibition involving the sleep centres. He was critical of Wilson's views that epilepsy and narcolepsy might have some common physiological basis and he emphasized the associated features of hypnogogic hallucinations and nocturnal weakness.

In a rather sarcastic article, JELLIFFE (1929) took a similar stand to Wilson. He considered that the creation of diagnostic categories without sufficient pathological/

/pathological foundations was a refuge of the ignorant and cites the use of 'genuine', idiopathic', 'essential', 'pseudo', 'true', 'pure', 'near', prefixes to diagnoses as evidence of this trend. Painting a rather florid picture he postulated that the clinician's experience of the syndromes of Narcolepsy, Hypnolepsy, Pyknolepsy was like viewing a well wooded region from the air, so that while some aggregation into discrete copses could be seen the trees essentially merged and formed links between one collection and the next.

Despite these criticisms of the validity of the concept of 'idiopathic narcolepsy' the syndrome continued to be supported by a series of extensive reviews over the next decade.

LEVIN (1929) attempted to reclassify the existing case material and added a number of his own cases. He advocated the generic term of 'morbid somnolence' which could be divided into:-

1. Morbid somnolence without cataplexy, i.e. a heterogenous group including patients suffering from tumour, vascular disease, encephalitis, metabolic and endocrine diseases, epilepsy and hysteria.
2. Morbid somnolence with cataplexy, i.e. Gelineau's syndrome.

Levin was particularly anxious to avoid any of the confusing concepts which had complicated the use of the word narcolepsy and also to avoid the use of 'symptomatic/

/'symptomatic narcolepsy' for his first group. He ran into the usual problem by this use of cataplexy as a dividing symptom - that there were people who suffered sleep attacks but had no cataplexy which he felt could be 'early cases' of Gelineau's syndrome but could not be kept with this group.

CAVE (1930) published a large series of cases (forty-five) collected from the records of the Mayo Clinic. He supported the use of cataplexy with sleep attacks as a diagnostic category and separated these attacks from epilepsy. Cave also agreed that sleep attacks were variable and cataplexy was often absent for periods so that careful history taking was required to establish the diagnosis. He was particularly emphatic that narcolepsy should be seen as no more than an unusual disturbance of normal sleep.

LEVIN (1933) again drew attention to the use of additional symptoms in the diagnostic criteria for narcolepsy. He pointed out that Wilson (1928) had recorded from his narcoleptic subjects a complaint of sleep paralysis which he saw as a form of nocturnal cataplexy in that there was a loss of muscle power but consciousness was retained. This symptom was originally described by Weir Mitchell (1876) in non-narcoleptic subjects but had been associated with narcoleptic sleep by several French and German neurologists (LHERMITTE, 1928; ROSENTHAL, 1927, 1928), both when going to sleep at night (pre-dormital) and during the night.

Levin showed that this state was associated with hallucinations and nightmares, and coupling this with the frequent clinical illustrations of how narcoleptics going into sleep attacks continued their activities for a while in a drunken way, discussed the syndrome as a state of 'partial sleep'. Leaning heavily on Pavlov's views he postulated that areas of inhibition occurred which separated the components of the sleep state and produced dissociation between "motor" and "consciousness" functions. This was the 'localized sleep' hypothesis.

NOTKIN and JELLIFFE (1934) also produced an exhaustive review of the published cases. They divided the recorded cases into five groups:-

1. Prolonged hypersomnia.
2. Hypersomnia secondary to cerebral disease.
3. Group associated with epidemic encephalitis.
4. Group in which epileptic and narcoleptic symptoms co-exist.
5. Cryptogenetic group of narcolepsy - without any evidence of underlying pathology.

While discussing the problem of the association of narcolepsy and epilepsy, these authors took the middle course of suggesting that information was inadequate for dogmatic assertions, and they considered that it was undesirable to consider narcolepsy as a disease but rather as a cluster of symptoms which could be produced under a variety of/

/of conditions. Narcolepsy and epilepsy on many grounds seemed to have features in common.

Another extensive review was made by DANIELS in 1934. From the Mayo Clinic cases and many of his own observations Daniels discussed in some length the cluster of symptoms which built up the clinical picture of narcolepsy and examined each in relation to his population. He found that sleep attacks and cataplexy were the commonest symptoms while sleep paralysis, hypnagogic hallucinations, nightmares with disturbed sleep, obesity and endocrine disorders were common but not obligatory symptoms and signs. Symptomatic cases did not differ drastically from idiopathic cases which Daniels took to mean that a variety of pathological process produced their effects because of physiological connections in the nervous system. He saw all the possible agents affecting the sleep regulation mechanisms lying in the floor of the third ventricle and suggested that 'idiopathic' narcolepsy might be due to a trivial encephaliac illness which never gave serious symptoms at the time of the original infection. This idea had already been put forward by LHERMITTER and ROUQUES (1927).

Daniel's paper is a model of careful evaluation of the history of each patient and he makes the point that it is not always easy to decide whether an incident - for example a head injury, is a cause of sleep attacks or whether the sleep attacks are being dated to the incident as a confenient/

/convenient definative historical event.

HALL and LE ROY (1936) came back to this problem. They pointed out that there was no report of a case of traumatic narcolepsy before 1917 and imply that the War and the epidemics of encephalitis have made clinicians look more carefully at sleep disorders. Calling up the observation of OSNATO and GILIBARTI (1927) that diffuse changes resembling encephalitis may follow concussion, they examined the incidence of post head injury narcolepsy, in their own cases and from the literature. Both sleep attacks and cataplexy were found associated and some cases of sleep attacks alone occurred. They imply that as head injury is a relatively common accident many cases of 'idiopathic' narcolepsy may be explained in this way.

During the period when these comprehensive reviews of the problems of narcolepsy and marked somnolence were appearing i.e. from 1926-1933 and the 'trivial cerebral damage' concept of the ~~idiology~~ aetiology of the condition was developing, a research instrument was being developed. HANS BERGER in a series of papers (1929, 1930, 1932, 1933, 1938) was describing his pioneering experiments in recording the electrical activity of the human brain. Early in his experiments he noted that the electroencephalogram varied in epileptics as though many neuronal groups were firing synchronously. Many workers followed up Berger's observations and by 1935, GIBBS, DAVIS and LENNOX had described the classical 3 per sec spike and wave/

/wave complex of petit mal, so that in theory a method was available to distinguish between epileptic attacks and other episodes of loss of consciousness.

BERGER (1930) had also noted changes in the encephalograph during sleep with the appearance of slower activity. Further experiments by Davis, Harvey and Loomis allowed the development of a classification of the changes of the encephalogram during sleep, (DAVIS et al. 1937; Loomis, 1937), and it was quickly found that there was little or no difference could be found between the sleep of the sleep attack and normal nocturnal sleep (BLAKE, 1939; JANSEN, 1939, GIBBS et al. 1935; GIBBS and GIBBS, 1941).

However, although the way was apparently clear to subdivide narcolepsy from epileptic disorders, there were great practical difficulties which made the electroencephalograph difficult to use to investigate individual cases. Early instruments were particularly unreliable and the records were very prone to contamination from outside interference. So while workers could examine the sleep changes as they occurred in a subject sleeping in the EEG laboratory during the day, over night sleep records were very rare.

The first study of narcoleptic sleep was carried out by BLAKE (1939). In association with Nathaniel Kleitmann these workers examined the EEG changes in normal and narcoleptic subjects, as well as in sleep deprived subjects and subjects receiving Benzedrine or alcohol. The eleven narcoleptics/

/narcoleptics showed marked drowsiness and slept readily in a recumbent situation. No evidence of epileptic changes was discovered.

A systematic study of narcoleptic sleep was made by Dynes and Finlay in 1941. Records taken from a group of 22 narcoleptic subjects showed that under the recording conditions the subjects were sleepy and all 17 subjects in the 'idiopathic groups' had normal waking records and went into stages of 'light sleep' very quickly. Five subjects with a diagnosis of 'symptomatic narcolepsy' usually those who had suffered from encephalitis, had abnormal waking records and did not go to sleep during the recording. Dynes and Finlay suggested that this was evidence in favour of a division into idiopathic and symptomatic groups and further that idiopathic narcoleptics suffered from a dysfunction of normal sleep mechanisms. It is also noteable that the bulk of cases who did sleep during the recording remained drowsy or in 'light sleep' - i.e. stages B and C of the Loomis classification which will be described fully in the next section.

GILL (1941) considered that the term narcolepsy was at that time being used for cases in which there are uncontrollable attacks of sleep, often without known cause. Reviewing the multiple examples of cerebral pathology which had been recorded to produce sleep attacks and cataplexy, he favoured Daniel's theory that attenuated attacks of/

/of encephalitis may be the pathological basis of the idiopathic syndrome and therefore Wilson's view that narcolepsy was a symptom complex, not a disease, was justified.

An interesting approach to the problem was made by BROCH and WIESEL (1941). They saw Narcolepsy as an intermediate state. Sleep was considered to be divided between physical sleep with tonelessness, areflexia, slowed respiration and pulse; and mental sleep or stupor. The normal individual was thought to sleep both mentally and physically, but the narcoleptic might sleep physically ant not mentally as exemplified by cataplectic attacks. Other states of dissociation would occur in sleep talking and sleep walking episodes, sleep paralysis and 'sleep hallucinosis'.

This dissociation was thought to be due to a localized neurological lesion in the posterior hypothalamic - mesencephalic area.

The relationship of narcolepsy to epilepsy was discussed by COHN and CRUVANT (1944). In their series of ten cases, minor neurological signs were noted, and the finding of high voltage slow waves during records when the subjects were considered awake was compared with the appeatance of inter ictal slow activity in the resting records of some epileptics. Sleep attacks during the records were accompanied by EEG signs of normal sleep and these authors revived the view of Foot and Singer in resurecting the term 'Hypnolepsy' to record the sleep aspect of the syndrome.

They concluded that the place of narcolepsy was in the family of epileptics as Wilson had suggested in 1928.

Wilson's views on narcolepsy were also taken further by FABING in 1946. He took the view that Wilson's concepts of a ~~Pelvic~~ Pavlovian wave of inhibition involving the brain stem and cortex in varying degrees did on a phenomenological basis account for all the classical narcoleptic symptoms, but left two unanswered questions.

1. Why did emotional experience produce central inhibition?
2. What was special about the brain of a narcoleptic which made it so susceptible to waves of inhibition?

In the first case, Fabing took Pavlov's later experiments and saw the emotional trigger to cataplexy as an illustration of the 'ultra paradoxical phase' in which repeated or overwhelming stimuli can produce paradoxical effects, i.e. inhibition as opposed to excitation. Emotional stimuli demanding a massive response could be seen in this light. However, Fabing was unable to understand why narcoleptics were susceptible to such inhibition.

The controversy over the finding of slow activity in the routine encephalogram of narcoleptic although they appeared awake continued well after this date.

Many studies agreed with the findings of DYNES and FINLAY (1941) in finding no evidence suggestive of inter ictal records in narcolepsy. (BLAKE, 1939; HEYCH, 1954; GASTAUT and ROTH, 1957; ROTH, 1961).

Others took the view that narcolepsy represented an equivalent state to epilepsy (ROTH, 1946, STAYSEL, 1950; BJERK and HORNISHER, 1958; LUGARESI, 1961). ROTH (1946) carried out electroencephalographic studies on one patient who showed clear episodes of spike and wave discharges as well as sleep attacks.

Psychosomatic approaches

Arising primarily out of the cases of morbid somnolence of prolonged duration, i.e. the 'somnosis' of Gowers, a number of authors considered sleep as a defense against stress and gradually short lived sleep attacks came to be considered in this way.

JANET (1921) described a case from the Salpetriere - a young girl who clearly described how when placed in a stressful situation - "when the illumination is too brilliant, or there is too big a crowd, or when I must do anything that is fatiguing or enervating; in a few minutes, I am gone; I do not know what I am doing, I act like a somnambulist, an automation". With severe attacks she would sink into a chair and fall asleep. Janet saw the prolonged sleep as a state of psychoasthenic depression with a 'delusion' of sleep. Sleep as a defense was clearly described by WILLEY in 1924, in the case of a young student who enjoyed drowsiness as a state in which his sexual fantasy was allowed full freedom - literally day dreaming when faced with unpleasant jobs like studying. At the time/

/time the student was involved in a difficult heterosexual relationship and sleep allowed a pleasant retreat from the difficult problems. In the same vein, SOLOMON (1928) described how repeated episodes of morbid somnolence could be related in his patient to periods in her life when the level of stress was high and there was no practical answer. Emotion was a clear precipitant of attack - but the emotions were of anxiety and depression - never laughter. This subject proved easy to hypnotize and an abdominal operation which was required was carried out under hypnosis. Finally under hypnosis it was suggested that she could produce the sleep on herself by autohypnosis after which sleepy episodes disappeared.

A full case report by MAXWELL JONES (1935) from the Royal Edinburgh Hospital describes episodes of prolonged sleep in a young girl which were connected with difficult relations and problems in the home environment. Other symptoms of conversion hysteria were found and Jones postulated that many of the narcoleptic symptoms could be understood as episodes of dissociation (using dissociation in the way Wilson used inhibition).

The transition from considering the psychopathology of prolonged sleepers to narcoleptics was made by MISSRIEGLER (1934). He showed that narcoleptic attacks in his patient were connected with conflicts arising from an early sexual relationship between the patient and his/

/his stepmother with which the patient was overwhelmed.

A more systematic approach was made by LANGWORTHY and BETZ in 1944. In a discussion of six cases they showed that narcoleptic symptoms occurred against a background of interpersonal problems often related to close family members. Usually a crisis or some increase in the difficulties was a precipitant of the sleep. Sleep attacks achieved secondary gain and attention could be focused on 'illness' rather than interpersonal problems. The problems in these cases were frequently a need to change the pattern of the individual's life from that of his parents and the symptoms of frigthening dreams and hallucinations were thought to be related symbolically to anxieties arising from the interpersonal difficulties.

While this paper serves admirably to point out the gain from symptoms it fails to suggest why the narcoleptic symptoms were 'chosen' by their patients from the much more common neurotic symptoms.

SPIEGEL and OBERNDORF (1946) reported on a single case observed over an extended period of time in hospital. A number of symptoms of conversion hysteria were present and it was found that attacks of sleep could be provoked by a rise in the level of stress around the patient. Exploration eventually revealed an incestuous relationship and disturbed sexual relationships in later life, and in the discussion a case of drowsiness in response to anxiety/

/anxiety and stress reported by Oberndorf in 1916 was recalled. ROTH (1946) also reported a case of narcolepsy (who also showed spike and wave cerebral discharges) in which the patient was thought to be escape by means of the attack from difficulties arising from relationships with a dominant mother in which the patient felt trapped.

The problem was reviewed by COOLEY (1948). He pointed out that many reviews had included cases in which psychological difficulties were prominent, and had considered that personality difficulties and changes in attitude often accompanied the narcoleptic illness. Analytic treatment started with a narcoleptic revealed increasing interpersonal problems and difficulty with sexual identity.

In an experiment approach to the psychological genesis of sleep attacks and cataplexy, BAKER (1948) endeavoured to raise the anxiety level in an abreaction technique using sodium amytal under conditions using an EEG monitor. Sleep was precipitated whenever the abreaction moved to emotionally laden areas.

They found evidence in favour of the theory that the narcoleptic is an individual 'caught' in a dependant situation which he tries to reject.

The concept that sleep symptoms could be psychosomatic was used by DRAKE (1949) in his review of the literature about narcoleptics in relation particularly to those/

/those in Army service. Sleep attacks were found to be associated with states of emotional conflicts but also in states of boredom.

POND (1952) in a concise review of the aetiological theories of narcolepsy made the point that in general, cases were seen by neurologists rather than psychiatrists and therefore included under the general heading of convulsive disorders even though no pathological basis for the condition emerged from neurological investigation. Psychiatrists saw few examples of the condition but clear observation existed of gain from sleep attacks. Further Pond argued it was certainly possible for psychological and physiological changes to be present simultaneously in individual patients so to assume that organic aetiological factors and psychological precipitants were mutually exclusive was illogical.

As a group, Pond found his cases to be narcissistic without energy and passive, frequently over dependent on one or other parent. Secondary gain was obviously ~~by~~ a factor, but secondary gain may be produced by a most chronic illness. Pond suggested that narcolepsy might be best seen as a disorder in vigilance. He considered that the EEG slowing found in routine records on his group of narcoleptics were signs of early sleep and that 'organic' changes were only likely in one case. He determined the convulsive threshold using Metrazol (GASTAUT, 1950) in some patients and/

/and found it normal. An episode of paralysis during a routine record was found to be associated with slowing of the EEG indicating drowsiness.

In an EEG study of one case in which continued drowsiness with sleep attacks followed on the development of rheumatic heart disease, VIZOLI and GIANCOTTI (1954) showed that paroxysmal activity accompanied drowsiness, and they considered this as evidence that narcolepsy was involved in the convulsive disorders. The patient did not suffer from cataplexy or any of the associated symptoms of narcolepsy. Also in 1954, Sir Charles Symonds made a spirited attack on the concept of cataplexy, pointing out that while many patients suffered from cataplexy with sleep attacks, cataplexy alone was possible and not necessarily a narcoleptic symptom. Symonds commented on the difficulty in distinguishing cataplexy from authentic epilepsy; cataplexy he considered as a varient of myoclonic epilepsy. Further 'drop attacks' were frequently confused with cataplexy and while these might not be epileptic in nature and the resemblance between cataplexy and drop attacks may be explained in physiological terms by the involvement of parts of the brain stem in both disorders. Thus on clinical grounds Symonds saw no fundamental distinction between epilepsy and cataplexy and considered that other types of seizure related to cataplexy might also be epileptic variants.

In the development of concepts of the narcolepsy syndrome one problem recurs regularly - what is sleep?

It is clear that many states of unresponsiveness and anergia may be classified phenomenologically as sleep. Thus it is obvious that many cases of cerebral pathology and also of psychosis confused early observers. The advent of the encephalograph and greater information about the EEG changes in epilepsy and narcolepsy failed to remove narcolepsy from the convulsive heading.

Before considering the next decade of thoughts on narcolepsy a better answer to the question of the definition of sleep is required.

III. What is sleep?

It has always proved very difficult to give a definition of sleep that was acceptable from all angles. Original workers saw sleep as a very 'negative' state, defining sleep as a 'state of inertia and unresponsiveness'. But inertia is a very relative term as people may move frequently in sleep, and responsiveness can be extremely selective - arising to a baby's first whimper but sleeping through a thunderstorm are claims frequently made by mothers. Nevertheless responsiveness was the clinician's criterion in the situation, but it was apparent before the turn of the century that all states of unresponsiveness were not sleep - for example Gairdner's patient (1884) was shown to snore during the night but not in the day - 'a sleep within a sleep' as he described it. So words like catalepsy, trance and stupor emerged to avoid the concepts attached to sleep. Confusion was also increased by the patient's testimony that during the sleep attack they might remember at least something of what was going on while they appeared to be asleep; and during cataplexy, or sleep paralysis, they claimed also to be wide awake but behaviourally inert or paralysed. This produced the necessity of dissociating one part of sleep from another, i.e. mental life from physical accompaniments of sleep.

The changes in the electroencephalogram during/

/during arousal and sleep did not initially prove of great assistance in the problem of sleep in narcolepsy.

LOOMIS (1937) described cyclical changes in the brain potentials which allowed him to advance a classification of sleep into reasonably definite stages on a five point continuum.

His stages were:-

a) Interrupted alpha rhythm, 9-11 cps, approximately 60 uV. Seen in wakefulness or slight drowsiness on lying down, relaxed, eyes closed.

b) Low voltage patterns in which alpha rhythm has been replaced by small undulations. Characterized by sensation of floating and passing into definite sleep.

c) A spindle state which includes the appearance of traces of waves 14-15 cps, 20-40 uV superimposed on an irregular pattern of slow waves.

d) Spindles plus random patterns with additional delta waves of about 1/sec as high as 300 uV.

e) A random pattern made up of still slower and larger delta waves with spindles usually gone.

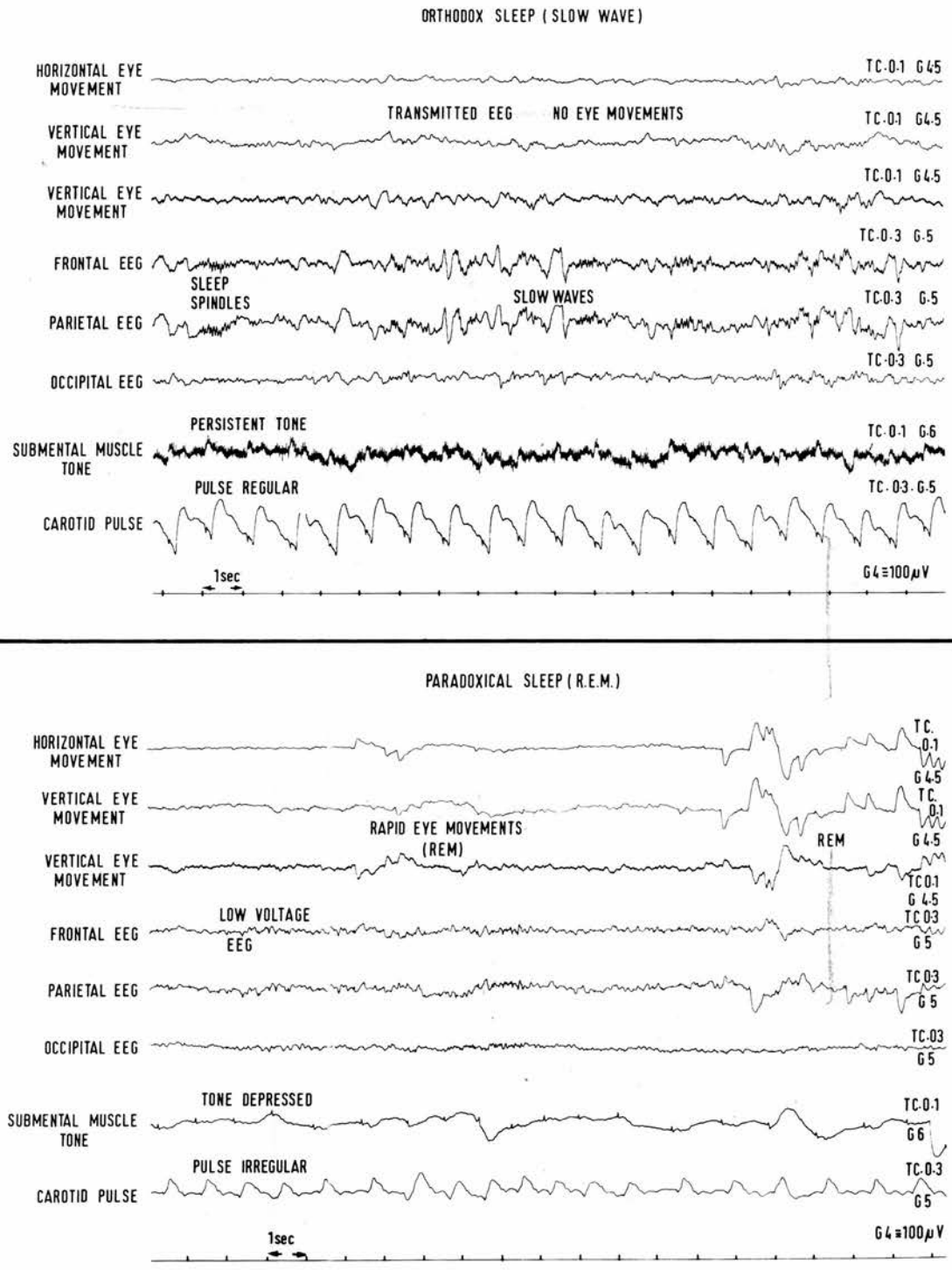
This pattern formed a series of repetitive cycles during sleep but it was noteable in retrospect that very little research into over-night sleep was possible during this formative period.

Narcoleptics were found to enter stage b) or c) very easily during routine records and the concept that/

/that narcoleptic attacks were essentially periods of drowsiness or 'light' sleep was current (DYNES and FINLAY, 1941). Although paroxysmal activity was absent from narcoleptic records, some slow activity was found in routine recordings and the similarity to inter ictal records was suggested by COHN and COUVANT in 1944.

The possibility that there was a different type of sleep was a frequent speculation in discussion on narcolepsy and was strongly put forward by McWILLIAM (1922) in his study of the fluctuations of blood pressure during over-night sleep. He found that during the night there were periods of great fluctuations in blood pressure which alternated with periods of regular, stable pressure.

However, the most significant advance was made by Kleitmann in 1953. Working with a student, Aserinsky, he observed the behaviour of puppies initially and then babies. Kleitmann described three basic states in the baby. There was a stage when the baby was awake and responded to the environment. There was a stage in which the baby was clearly asleep, inert and unresponsive. There was also a third stage in which the baby remained unresponsive to the environment but moved, made sucking movements and also moved its eyes in a jerky fashion. Kleitmann considered both the second and third states to be sleep and called them 'passive' and 'active' sleep respectively. This observation led him to the question of whether these two states were present/



THE CONTRAST BETWEEN SLOW WAVE SLEEP AND RAPID EYE MOVEMENT SLEEP

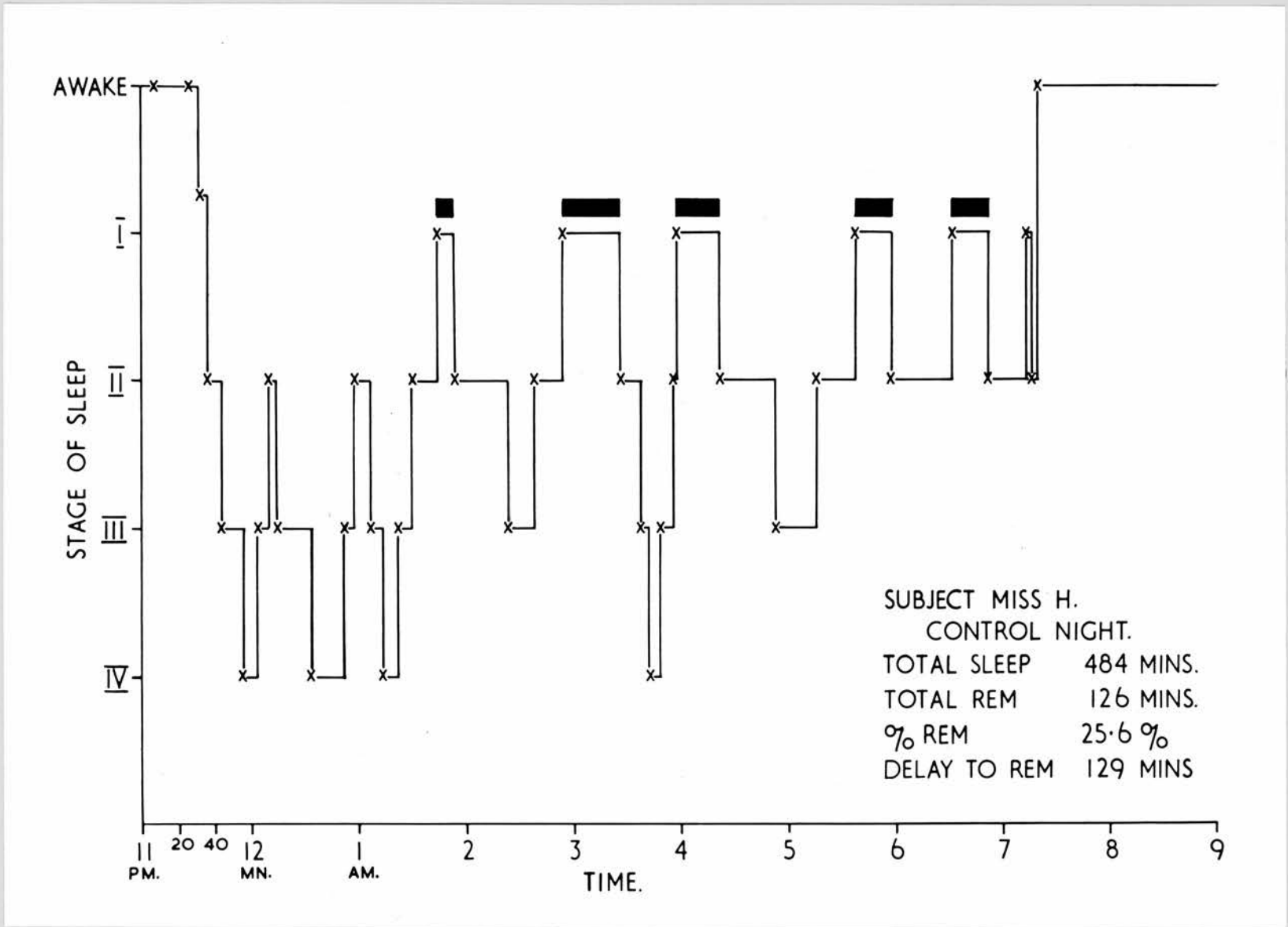
/present in the sleep of the adult. Basing the distinction on occular motility and using a periorbital method of recording the electro-oculogram, he began overnight records on some of his college students. Cycles of slow waves and spindles were identified and between the cycles of slow waves, jerking synchronous bursts of rapid eye movement were seen against a background of "b" type sleep - or emergent sleep. (FIG. I. Two types of sleep).

Kleitmann woke his subjects in slow wave sleep and in REM sleep and was able to show that dreaming was associated with REM sleep.

The first series of papers by Aserinsky and Kleitmann established REM sleep and started a massive renewal of interest in sleep.

In retrospect it is interesting that eye movements had previously been suggested to accompany dreaming by LADD in 1892.

Much research was devoted in the period 1955-1960 towards a better understanding of the connection between REM sleep and dreaming, and to a full investigation of the REM sleep state itself. By 1960 REM sleep had been shown to differ from slow wave or orthodox sleep in a multiplicity of different physiological and chemical parimeters and was established as a definite primitive state. Research works emphasized the independence of REM sleep by referring to this sleep as the 'third state' (SNYDER 1963) or as "two types/



A SLEEP HISTOGRAM OF ONE CONTROL SUBJECT. THE CYCLES OF SLOW SLEEP ALTERNATE WITH THE BLOCK (BLACK) OF REM SLEEP

/types of sleep" (OSWALD, 1962).

The association of REM sleep and dreaming was amply supported by repeated experiments although the association was rather variable in different series and dreams were recorded from orthodox sleep. (DEMENT, 1955; DEMENT and KLEITMANN, 1957; FOULKES, 1962; GOODENOUGH, 1959; JOUVET, 1960 and SNYDER, 1965).

Very early in the development of the concept of this third state, Dement showed that similar physiological changes were present in the cat (DEMENT, 1958) which opened up even greater neurophysiological investigations of this state in an animal preparation (JOUVET, 1960). The physiological changes which occur during REM sleep and serve to differentiate it from slow wave sleep already form an extensive series.

In Summary:-

Variable	Orthodox or slow wave sleep	Paradoxical or REM sleep	Authority
PULSE RATE	Regular Slowed	Frequently irregular with runs of tachycardia and occasional bradycardia.	Aserinsky and Kleitmann, 1953. Snyder, 1965. Snyder et al. 1964.
BLOOD PRESSURE	Usually lowered and stable	Systolic elevation Greater fluctuations	Candia 1962. Snyder 1963. Bristow, 1969.
RESPIRATION RATE	Regular	Fluctuant rate Periods of apnoea with intervals of tachypnoea.	Snyder 1965. Aserinsky, 1967.

MUSCLE TONE IN SUBMENTAL REGION	Low but persistent level in Stage IV sleep.	Drops to zero before appearance of REM sleep.	Berger, 1961.
MOVEMENT	Distributed over-night	Excess of small facial and other small movements during REM sleep	Roffwarg, 1964.
PENILE ERECTIONS	Flaccid	Full or partial erection during REM period.	Fisher, 1965.

The discovery of REM sleep in cats (DEMENT 1958) has been followed by its identification in a wide range of mammals ranging from the rat (MICHEL, 1961) to the opossum (SNYDER, 1964). This has opened the way to a greater neurophysiological understanding of sleep.

Sleep as an active process

The pioneering experiments of BREMER (1935, 1936) demonstrated that transection of the cat brain at the level of the foramen magnum (the 'encephale isole' preparation), was compatible with alternating cycles of sleep and wakefulness. However, transection at a high diencephalic level - the 'cerveau isole' preparation was only compatible with sleep. On this evidence it could be hypothesized that there existed in the brain stem an alerting mechanism which woke the sleeping brain periodically and was inoperative in the cerveau isole preparation. This alerting mechanism was identified with the non-specific projecting system arising from the brain stem reticular formation as/

/as described by MORUZZI and MAGOUN in 1949.

Sleep in this model could be seen as a withdrawal of the activating influence of the reticular formation arising from its multiple inflow of sensory stimulation via the cranial nerves (ROGER, 1956).

Unfortunately many observations indicated a more definative sleep producing role was present in hypothalamic and in brain stem areas. HESS (1949) described one instance in which behavioural sleep was produced in a cat by low rate stimulation of midbrain structure. This was later confirmed by PROCTOR (1957). Cataleptic symptoms with somnolence were observed following electrical stimulation of the pontine reticular formation of the awake, freely moving cat by BURGI and MARINER (1943). Direct high rate stimulation of the mesencephalon (INGVAR and SODERBERG, 1958) and low frequency stimulation of the medullary reticular formation (Favale, 1959) were found to produce EEG synchronisation.

Two fascinating experiments demonstrated conclusively that sleep promoting activity was localized to the brain stem. A mid pontine transection of cat brain produced a preparation which prescribed a great preponderance of wakefulness - more so than the encephale isole with its significantly greater afferant input. (BATINI, 1958). The experiment suggested that structures in the caudal brain stem were exercising a synchronizing effect on the cerebrum. MAGNI (1959) showed that small doses of sodium thiopentone injected into the/

/the vertebral circulation could produce EEG arousal in the sleeping cat, whereas injection into the carotid circulation produced EEG synchronization in the alert cat after division of the posterior communicating artery. Thus there is ample evidence of a sleep promoting 'centre' in both the candal brain stem and in the hypothalamic/mid brain area.

The balance between the alerting arousing reticular system and the synchronizing sleep promoting centres can be seen as a satisfactory model for the production of slow wave or orthodox sleep, and MORUZZI (1961) was able to demonstrate that the sleep promoting centre in the candal brain stem was connected with the input from baroreceptors in the carotid arteries which when stimulated had been shown to promote sleep (KOCH, 1932).

This neurophysiological model appears to explain the onset of sleep and arousal from sleep, very well. However the discovery of a second type of sleep - REM sleep posed more of a problem. Did this type of sleep have a different neurophysiological mechanism or was it a variant of the existing mechanism?

Much work has been done to elucidate this problem by JOUVET (1961, 1963). Jouvet set out to test the compatibility of the 'deafferentiation' theory of sleep with the diencephalic sleep centre theory of Hess. He pointed out that it was no longer possible to set criteria of sleep/

/sleep by EEG cortical activity as the REM sleep described in the cat by DEMENT (1958) was a sleep state in which the EEG activity was little different from an aroused EEG. He considered REM sleep as a form of 'activated sleep'. Further he considered that cats after brain stem damage may show EEG slowing compatible with sleep but continue to show peripheral responses more in keeping with arousal. So in his research he determined to include in his estimate of sleep as many central and peripheral indicators as possible.

Initially Jouvet confirmed the presence of REM sleep following a period of slow wave sleep but further he found that while the EEG of the cat in REM sleep was indistinguishable from the awake record, spindling activity at 6-8 cps was prominent in the pontine reticular formation - and it was because of this 'hind brain' sleep, Jouvet christened REM sleep 'paradoxical sleep'. Peripheral changes such as the loss of EMG activity in some muscles and a reduction in evoked activity from cortex and subcortical structures was noted. Small jerking movements involving facial and tail muscle accompanied the synchronous bursts of eye movements so that the REM sleep state seemed closely identified with human REM sleep.

These central and peripheral findings were not influenced by removal of cortex or cerebellum, although decerebrate rigidity was abolished in the REM sleep state.

Total removal of neocortex had the effect of abolishing evidence of spindling activity and slow waves, while slow spindling activity could still be recorded in the central pons during REM sleep, which pointed to the changes of slow sleep (or orthodox sleep) being cortically derived.

Cortex and subcortex above the level of section in the cerveau isole preparation showed persistent slow waves and spindles whatever the state of 'wakefulness' shown by peripheral responses. While the brain stem and peripheral changes in REM sleep were unaltered in this preparation eye movements were sparse.

Sedtion of the brainstem at the level of the lower pons abolished the peripheral signs of loss of tone, heart rate changes and changes in respiration, while the activity in the pontine reticular formation was severely attenuated, spindling could still be found on occasions.

The concept that there existed in the region of the pons a centre which was responsible for REM sleep seemed the logical explanation of this data.

Proof of this hypothesis required more detailed coagulating experiments. In the course of this work it was found that damage to the posterior part of pontine reticular formation adjacent to the superior vestibular nucleus - the nucleus pontis candalis, produced a preparation in which no REM sleep could be identified during its survival time although orthodox sleep and arousal could be observed.

The connections of this pontine centre with the cortex proved to be outside the normal ascending activating system, as Jouvet demonstrated that section of the reticular formation at the level of the midbrain tegmentum abolished arousal, but not the fast activity of REM sleep, as long as the central midbrain was intact and the inter-peduncular nucleus and mammillary bodies undamaged.

On theoretical grounds Jouvet considered that the link was with the limbic midbrain circuit described by NAUTA (1958).

The behaviour of cats with a lesion involving the caudal pontine reticular formation was of great interest, in that despite the lack of paradoxical sleep, they showed behavioural changes, periodically they would have a fixed gaze with head up and pupils dilated and they would reach out with their paws as if attempting to touch an object. (JOUVET, 1963). Jouvet likened these episodes to 'hallucinatory states'.

Jouvet considered that the physiological changes in the periphery were due to the activity of the inhibitory lower reticular formation nuclei and their close anatomical links with cardiac and respiratory centres.

The function of the limbic system and its connections in sleep is still uncertain. While many workers have shown the presence of a prominent 5-6 cycles/sec activity in the hyppocampus of both cat (GRASTYAN, 1961) and man (BANCAUD, 1964), supporting Jouvet's suggestions of the activity/

/activity of the system in REM sleep, other workers have postulated that within the connections of this system and the frontal cortex exists a centre which actively promotes slow wave sleep. (HERNANDEZ-PEON, 1963, NAUTA, 1946).

Another interesting pathway involved in REM sleep has seen outlined by BROOKS, 1963 and JOUVET, 1965. Spike activity in the pons, occulomotor nuclei, lateral geniculate body and occipital cortex (P.G.O. spikes) link brain stem and cortical visual centres. This activity coincides with and most frequently antidates the eye activity which gave the state its customary name and appears to be exclusively associated with the REM sleep state. It seems that those P.G.O. spikes will be a most useful central indicator of REM sleep.

One most impressive conclusion which arises from the ~~multitude~~ multitude of neurophysiological papers of work done on REM sleep is that the level of cerebral activity during REM sleep is at least that of arousal and often greater than arousal. This fact has been shown in single neurones, (EVARTS, 1964; HUTTONLOCHER, 1961), visual cortex (EVARTS, 1962), subcortical structures (JOUVET, 1959) as well as in the visual pathways. The concepts of REM sleep as 'active' sleep (ASERINSKY, 1953) seems very justified in regard to brain activity.

One further point arising from the work on different animals is that although the cycle of slow sleep-REM sleep/

/sleep varies from 3-4 minutes in a mouse, to 120 minutes in an elephant and seems to be linked to metabolic rate, (HARTMANN, 1961) REM sleep always follows a period of slow wave sleep.

REM sleep has been identified in many animals and while the list is not complete, it is suggestive that it has not been identified in fish and only transitory episodes which ought to be REM sleep has been found in birds (HARTMANN, 1967). Although it is so wide spread in the animal kingdom there are differences in the various features of the state between species.

In Man, REM sleep is over prominent at birth and during the first two years of life (PARMALLEE, 1961) but throughout childhood, adolescent and adult life it is remarkably constant, declining slowly in old age. (HARTMANN, 1967). Throughout the bulk of adult life the average person spends apprxoimately 1.6 hour/night in this state - an average of 24% of total sleep.

There have been several studies which illustrate the persistance or the demand made by man for this state. Deprivation experiments in which subjects were woken at the start of each REM sleep period which kept the level of REM sleep down to 1 or 2 percent, (DEMENT, 1960, 1965) showed that when sleep was interrupted, an excess demand was made for REM sleep.

PATTERNS OF SLEEP

Stages of Sleep

Subject M4 (Idiopathic hypersomnia)

1. Awake. Traces of alpha rhythm posteriorly. Small rolling eye movements. Tone prominent Heart rate regular.

2. Stage I. Slow wave sleep. Polyrhythmic record with runs of slow waves. Pulse regular.

3. Stage II slow wave sleep. Sleep spindles (14 cps) prominent. Arousal response 'K' complex is synchronous. Tone persistant. Pulse regular.

4. Stage III slow wave sleep increasing slow activity. Tone persistant. Pulse regular.

5. Stage IV slow wave sleep. Record demonated by slow waves (1-3 cps). Tone persistant. Pulse regular.

6. REM sleep. Bursts of jerking eye movements. Low voltage EEG with some slow waves. Tone minimal. Slight pulse irregularity.

Similarly with hypnotics (OSWALD, 1965, EVANS, 1968), which depress REM sleep initially, a REM sleep excess or rebound was found when the drug was stopped which took several weeks to subside.

In the light of these discoveries, sleep can be defined as an active process, rather than a state of cerebral inhibition. Sleep is a complex state which consists of two alternating phases - one, orthodox sleep is characterised by regular physiological variables and slowing of brain activity; the other, REM sleep, by an increase in cerebral activity, and irregularity of physiological variables. Under normal circumstances both phases are clearly defined and orthodox sleep takes precedence over REM sleep.

The more recent discoveries in relation to sleep have changed some of the basic categories of the original classification of sleep (LOOMIS, 1937). DEMENT proposed in 1957 that the slow wave cycle should be limited to five stages, i.e.:-

Awake	with evidence of alpha activity, eye blinks and eye movement under closed lids
Stage I	(drowsiness) with disruption of alpha activity and the appearance of fast components and a few slow waves on the EEG.
Stage II	defined by the presence of sleep spindles (14 cps) and K complexes.
Stage III) Stage IV)	defined in relation to the amount of high voltage slow wave activity present.

Submental muscle tone was present although miminished throughout these sleep periods and eye movement was limited to slow rolling movements during drowsiness.

Stage REM — Jerking cynchronous eye movements, low voltage EEG with a few slow waves. Submental tone minimal.

These basic stages have been further developed and reconsidered periodically. By common agreement an international classification of sleep, revised at intervals is now the most used criterion (RECHTSCHAFFEN et al. 1968) (FIG. II).

IV. Recent concepts of Narcolepsy.

The expansion of knowledge about sleep made no immediate impact on clinicians concerned with the problems of narcolepsy.

SWITZER and BERMAN (1956) reported a case and reviewed the controversies of narcolepsy/epilepsy and idiopathic/cerebral damage aetiology. They came down in favour of a psychogenic basis for idiopathic conditions explaining the apparent increase in the syndrome on the basis of the stress of the World War I.

YOSS and DALY (1957) in an authorative paper reviewing the Mayo Clinic cases, attempted to lay down firm diagnostic criteria for the narcolepsy syndrome. They proposed a diagnostic tetrad of sleep attacks, cataplexy, hypnogogic hallucinations and sleep paralysis. In a further paper (1957) these authors showed that from an encephalographic viewpoint, narcoleptics seemed to be continually drowsy and the sleep attacks were an exacerbation of this state. They were firmly convinced that the slow activity noted by other EEG investigations (CONNAND CONVANT, 1944) were signs of early drowsiness rather than inter ictal changes. Drowsiness occurred within minutes of setting up the recording in the bulk of the patients, but more definite sleep changes (i.e. spindling activity) was rarely seen. They found no significant changes in the EEG during cataplexy and sleep paralysis episodes, and finally attributed the drowsiness/

/drowsiness to a reversible alteration in the reticular activity system.

A careful appraisal of the symptoms of the narcolepsy syndrome was published by GANADO (1958). He discussed narcolepsy as an alteration in the diurnal sleep wake regime with sleep both resistable and irresistable intruding into the day producing a lowered awareness, hallucination 'figure-like' states, tension, mental symptoms and physical symptoms such as diplopia. Sleep attacks and cataplexy were acute or subacute shifts in the intensity of these symptoms. Ganado referred to the concepts of the reticular activating system and coupling this with the 'hypothalamic' symptoms of obesity and autonomic instability, implied that narcoleptics suffered from a chronic inadequacy of the arousal system. He noted that while there was EEG evidence of drowsiness in most cases, frank sleep changes were rare and promoted Daly and Yoss' concept of the narcoleptic as a chronically drowsy person. The connection of emotion with the bulbar system and muscle tone with the caudal reticular system explained the cataplectic episodes. The lack of sufficient activity in the reticular system was ascribed to a neurochemical transmitter such as noradrenaline deficiency in that system, which Ganado correlated with the success of sympathetico mimetic drugs in the treatment of narcolepsy.

SMITH in a series of papers (1958a, 1958b, 1959b) explored the psychosomatic aspects of the problem of narcolepsy. He was impressed by the conflicting reports on the relevance of psychodynamics to sleep symptoms and raised the interesting point that there might be more than one population of narcoleptics and only the emotionally disturbed members were seen by psychiatrists. However, he was able to draw from the literature much evidence of emotional and personality disturbance in the group of narcoleptics. Smith carried out many tests on his two patients - EEG, studies of glucose metabolism, the Funkenstein test and essentially found no significant changes, but this left him with the feeling that there was some underlying metabolic dysfunction. Both approaches - psychosomatic and metabolic were investigated in successive papers.

In a valuable paper (1958b) Smith discussed the concept of psychogenic hypersomnia - a disorder which had largely disappeared from the literature as the last case had been reported by JONES in 1935. On clinical grounds Smith considered that there was evidence that many of the patients were suffering from psychiatric illnesses - hysterical dissociation, depressive stupor or coma, and schizophrenia were the likely causes. Physical examination, observation and EEG investigations often showed that the individuals were actually asleep for only part of the time (PAI, 1950; ROTH, 1957). Smith reported one case in which the/

/the periods of 'sleep' showed evidence of relaxed brain activity and there was no significant differance between the EEG whether the patient was 'awake' or 'asleep'.

As the sleep episodes in this case had originally been short lived, Smith suggested that many narcoleptic sleep attacks could be understood on a psychopathological basis.

Exploring the possibility of a metabolic cause for narcolepsy Smith (1959a) compared this disorder to alterations of consciousness produced by hypoglycaemia. He noted that hypoglycaemia appeared to diminish drowsiness in narcoleptic patients and confirmed this finding suggesting that the hypoglycaemia promoted the output of catecholamines to restore the blood glucose. As the reticular formation was sensitive to catecholamines, alerting resulted, but drowsiness returned when blood glucose levels were restored. This was further evidence of the involvement of the reticular formation in the production of sleep attacks.

Another approach to the understanding of the narcolepsy syndrome was made by BIRCHFIELD, SIEKER and HAYMAN (1958). It had been shown that drowsiness and sleep were associated with a fall in oxygen tension and a rise in pCO_2 values (MANGOLD, 1955, ROBIN, 1957).

BIRCHFIELD et al (1958) confirmed these blood gas alterations which they suggested were due to hypoventilation and a reduced sensitivity of the respiration centre to gas tensions. Narcoleptic subjects however showed CO_2 retention/

/retention and mild anoxia while awake and the changes with sleep were less definite. These views were not supported by BULOW and INGVAR (1963) who reported on a study of four idiopathic narcoleptic patients, all of whom also suffered from cataplexy. Bulow and Ingvar's method of analysis of alveolar pCO_2 allowed them a breath by breath readout and they were able to show that while their narcoleptic patients were very drowsy people who slept readily in the recording situation, while they were roused, ventilation was normal and pCO_2 levels within the normal range. Thus Birchfield's data was simply due to the effects of drowsiness.

Curiously the greatest advance in the study of narcolepsy comes from a psychiatric orinetated project which stimulated neurophysiological investigation. VOGEL (1960) considered the function of the sleep attacks. As seen by other workers they arose at a time of mounting tension (LANGWORTHY and BETZ, 1944) or a time for a strong repression of feeling (SWITZER and BERMAN, 1956). BARKER (1948) had described how a sleep attack had occurred during analysis which a partciuarly painful fantasy was brought out, and Spiegal had reported how pathological sleep could be seen in his case to be a defence against strong guilt feelings.

Exploring this role in his patient, Vogel concluded that "narcolepticsattacks provide hallucinatory gratification of forbidden fantasies by the specific mechanism of wish/

/wish fulfillment through dreaming". This suggestion revived the older observation that many narcoleptics recalled dreaming during even short lived sleep attacks (DANIELS, 1934; DRAKE, 1949).

In association with Rechtschaffen, the diurnal sleep and the nocturnal sleep of this patient was monitored and REM sleep was clearly identified at the start of the sleep process. Rechtschaffen tested this correlation further and reported in 1963 that in seven out of the nine narcoleptic patients whom he had studied, REM sleep onset occurred at the start of the night's sleep, and REM sleep onset was noted in one narcoleptic diurnal attack. The total amount of REM sleep in these subjects was not significantly changed by the period of REM sleep at the beginning of the night from the amount found in normal controls. But the amount of the "deeper" stages of slow wave sleep (Stage III and IV) was reduced and narcoleptics proved to be more restless than normals during the night. This observation was confirmed by TAKAHASHI and JIMBO (1963) who found SOREM[+] periods in the sleep of eight out of ten idiopathic narcoleptics.

In 1963 SOURS reported on his findings in a retrospective study of 115 vases of narcolepsy. This is the most recent of the large surveys which illustrates many of the clinical findings. In this group 75 were considered idiopathic and 13 symptomatic narcoleptics. 19% complained only of sleep attacks; 72% had some cataplexy symptoms; and only/

[+] Sleep onset rapid eye movement

/only 11% presented and full tetrad of YOSS and DALY (1957). Male subjects were over represented by 3.2; and the mean age at onset of the disorder was 18.2 years and was thought to be related frequently to puberty. In nine patients there was a family history and in all cases cataplexy was a later symptom than sleep attacks. Weight gain and growth changes were common in the start of the illness, and headaches, anxiety, depression, instability and personality problems were common in the group. This predominent personality pattern was of a passive-aggressive type. The range of physical symptoms seen in association with the group was very large and inconsistent.

Of the symptomatic narcoleptics, cerebral damage, post encephalitic illness, lead encephalopathy and spontaneous hypoglycaemia due to a pancreactic adenoma were found. Psychotic stupor was also reported in the symptomatic group of narcolepsies.

Somewhat in contrast with the findings of Rechtschaffen (1963) NIXON et al (1964) studied the sleep of two adolescent narcoleptics with matched controls and found that REM sleep was less than 10% of total sleep (23.7% of total sleep in controls). Medication was stopped at the time and the results were based on four night recordings taken at intervals. No mention is made of any REM sleep onsets in these records and this report was so out of keeping with the more extensive series of Rechtschaffen that one can only/

/only suggest that some hidden factor - perhaps severe anxiety was influencing their results.

In the same year, DEMENT, RECHTSCHAFFEN and GULEVICH (1964) reported to the Association for the Psychophsyiological Study of Sleep, on the study of the narcoleptic attack. 16 male and 14 female patients with a diagnosis of narcolepsy were investigated. 22 subjects reported cataplexy, and all medication had been stopped before the recordings.

After an opportunity for a full night's sleep they were instructed to resist any sleep attacks and were recorded sitting in a chair, reading around midday. All fell asleep, and in 18 of the 22 patients who complained of cataplexy, REM sleep developed immediately. In 7 of the 8 non-cataplectic subjects slow wave sleep developed.

An attempt to resolve further the apparent connection between narcolepsy and epilepsy was made by KANEKO (1964). He utilized the concept of the sedation threshold (SHAGASS, 1954) which is the amount of a sedative drug (sodium amylobarbitone) given intravenously at a standard rate, required to produce a standard degree of sedation. As epileptics are tolerant of sedatives and narcoleptics intolerant of these drugs, the sedation threshold should differ - and Kaneko found the threshold was 1.8mg/kilo in narcoleptics and 3.5mg/kilo in epileptics. A convulsant drug was used to investigate the convulsive threshold of both groups of patients. Metrazole threshold was greater/

/greater than 6mg/kilo in narcoleptics and less than 6mg/kilo in epileptics.

On these grounds Kaneko and his colleagues felt satisfied that there was a different physiological basis for the disorders.

Two further papers emerging from this research school further clarified the narcolepsy problem.

In order of publication, HISIKAWA (1964) reported on alterations in electromyographic recording during sleep and the sleep of narcoleptics. They also investigated the H-reflex - a monosynaptic reflex induced by electrical stimulation of the tibial nerve in the popliteal fossa carrying afferent neurones from the calf muscles, and recording EMG response from the calf muscles. In a group of normal subjects and narcoleptics, recorded over night and in the day, submental EMG activity declined with slow wave sleep but was only absent at the start of REM sleep. The H reflex similarly declined with sleep, but decrease was maximal to the point of disappearance, only in REM sleep.

In the REM onset sleep found in narcoleptic patients the findings were identical, demonstrating that this REM sleep was identical with other REM sleep buried in slow wave sleep. When woken by the examiner from an "attack" of REM sleep in the day, two narcoleptic patients reported sleep paralysis and insisted they had been awake. Two other patients reported dreams in the REM onset sleep. While/

/While 'tonic' EMG activity disappeared during REM sleep these authors pointed out that 'phasic', i.e. intermittent episodes of muscle potentials are well developed during REM sleep and may correlate with the fine movements noted in this type of sleep.

In 1965 HISIKAWA and KENEKO published their findings on a large group of narcoleptics. Routine records showed persistent signs of drowsiness in the whole group although the subject might be actually performing a task such as overbreathing. In a subgroup of 21 patients more extensive recordings revealed REM sleep onsets in four cases, and REM sleep occurred with a very short latency (less than 20 minutes) in twelve other cases. However, REM sleep was not found despite some repeated recording in other cases in this group. Dreams or hallucinations were frequently reported when these subjects awoke and were awakened from REM sleep, and cataplexy was recorded on two occasions coincident with REM sleep onset. Sleep paralysis was also reported by subjects. These authors found the patients who reported sleep attacks, cataplexy and sleep paralysis, were more likely to show REM sleep onsets.

The EEG during a cataplectic attack was said to show a persistent alpha rhythm if the attack lasted a minute or less, but persistance beyond this was associated with the appearance of REM sleep.

This was the published data on narcolepsy at the time/

/time when I started to collect and investigate hypersomniacs. Further papers will be discussed at a later stage in this thesis in relation to my findings.

V. Other syndromes associated with hypersomnia.

1. Psychosis

It is abundantly clear that many of the patients with hypersomnia described in nineteenth century were likely to be suffering from a psychotic state. GAIRDNER's (1880) case of a 'trance' occurred in a puerperal period and could have been a depressive stupor which remitted spontaneously. EDWARDS' (1841) description of the behaviour of 'Sleeping Effie' suggests that she may have suffered from a manic depressive disorder. CREMEN's (1885) case of somnolence showed signs of flexibilitas cerea which was clearly not linked in the physician mind with the state described by KAULBAUM (1874) as Catatonia or Tension Insanity.

However the association of a definite narcoleptic state with a psychosis was first clearly described by DODS BROWN (1907) in the Royal Edinburgh Hospital. Sleep attacks, cataplexy, were clearly described, and the psychosis was noteable for marked hallucinatory experiences. Paranoid delusions developed under the influence of hallucinatory phonemes. An exploratory trephining operation was unhelpful, and his paranoid symptoms were related to the intensity of the narcolepsy attacks. Sedatives and excitements were said to be of no value. Brown stated that "it is easy to understand that delusional and impulsive conditions had their origin in hallucinations".

Despite this very clearly described case, a psychosis in association with narcolepsy was not recorded during the post World War I period when so much attention was being taken of sleep disorders, and in the collections of cases made by ADIE (1926) LHERMITTE (1927) WILSON (1928) no mention of psychosis occurs.

FRODERBERG (1930) reported a patient suffering from sleep attacks, cataplexy, vivid dreams and hallucinations prior to the development of paranoid delusions.

THIELE and BERNHARDT's case (1933) had shown previous religious tendencies before developing narcolepsy as an adolescent. He became excited and overactive, markedly hallucinated and increasingly paranoid and religious.

YOUNG and SCOVILLE (1938) reported three narcoleptic patients who developed paranoid hallucinatory illnesses but attributed the paranoid symptoms to the medication that their patients had received.

In Daniel's collection of narcoleptics from the Mayo Clinic (1934), one patient, a girl aged 14 suffered from sleep attacks and cataplexy. "Her dreams and hallucinatory experiences began to occur during the day as well as the night and the patient began to believe in their reality".

The case reported by LOCKE and BAILEY (1940) was interesting as auditory hallucinations antedated the narcoleptic symptoms by fourteen years. A paranoid state developed but insight and understanding of the patient/

/patient left the authorities wondering whether to regard this as a psychosis or a personality disorder.

Similarly in the case reported by BROCH and WIESEL (1941) the paranoid state appeared to develop from a 'peculiar dream state'. The authors noted some hysterical traits on this subject and had some doubts on the nature of the psychosis.

In 1943 LEHRMAN and WEISS described a paranoid reaction in a narcoleptic patient who was considered schizoid and over sensitive about her attacks of sleep and cataplexy. The clinical picture showed evidence of marked thought disorder and a diagnosis of schizophrenia was made.

In a case reported in his series of narcoleptics DRAKE (1949) made a diagnosis of paranoid schizophrenia with narcolepsy. Similarly QUENSEL (1952) commented on a syndrome of narcolepsy in association with mental subnormality in which the patient developed severe auditory hallucinations. A diagnosis of Propfschizophrenie - 'grafted' schizophrenic was made.

SMITH (1958) described a narcoleptic patient in whom a psychosis 'seemed to develop out of vivid nightmares'. A diagnosis of paranoid schizophrenia was made but again it was noted that this patient was 'remarkably detached and objective about her hallucinations'.

Two cases were reported by EILENBERG and WOODS (1962) who developed paranoid psychoses. Marked nocturnal hallucinations were prominent in the first case and a/

/a diagnosis of paranoid schizophrenia was made in this case. In the second case, considered as a schizoid individual, marked hallucinatory symptoms developed connected with sexual experiences. The authors were less happy to diagnose paranoid schizophrenia in this case as insight was retained and her experiences classified as 'dreams'.

COREN and STRAIN (1965) described a case of narcolepsy with psychosis where vivid dreaming antedated the psychosis. The authors were struck by a 'hysterical' quality in the narcoleptic symptoms which seemed to offer a gain to the patient. A diagnosis of a paranoid state was made. These authors are emphatic that the psychosis associated with narcolepsy cannot be explained by an unitary concept.

The difficulty arises on several fronts. Clearly there are psychotic episodes associated with narcolepsy which seem indistinguishable from schizophrenia in that marked thought disorder and no insight are prominent features of the disease.

Paranoid states arising in connection with vivid dreams nightmares and hallucinatory experiences, present a different clinical picture in which the hallucinations never seem to involve the personality completely so that insight is retained.

However there is no doubt that the frequent use of sympathetico-mimetic drugs to treat narcolepsy may increase the risk of paranoid illnesses in narcoleptics as it has been shown that these drugs can produce a paranoid/

/paranoid illness indistinguishable from paranoid schizophrenia in other patients (CHAPMAN, 1954). However it must be accepted that many narcoleptics continue to use these drugs without evidence of abuse or the development of paranoid symptoms.

COREN and STRAIN proposed that when the question of drug induced psychoses and schizophrenia had been investigated, the remaining paranoid states should be called the Paranoid States of Narcolepsy. These patients, they suggested were understandable in that these patients were subjected to continual vivid hallucinations until reality testing became impossible and a degree of belief in the hallucination occurred. However some insight always remained. The question of psychosis arises in connection with another 'syndrome' of hypersomnia.

2. <u>The Kleine-Levin syndrome</u>

This 'syndrome' developed by degrees from the reports of hypersomnia in the literature, adopting Gower's proposal that narcolepsy should be used to describe a state in which brief attacks of sleep interrupt the awake state, left a large and heterogenous group of sleepers - the 'somnosis' syndrome in which sleep was prolonged and the sleeper difficult to rouse. CARLILL (1919) described a prolonged sleeper, a boy of nineteen who was considered to be hysterical, and JANET (1921) described a similar prolonged sleeper in the Salpetriere who was considered hysterical.

In 1925 Kleine collected five cases from Kleist's Clinic under the general heading of periodic hypersomnia. Three cases were somnolent in association with the menstrual cycle, but two others were recorded to show increased appetite in the somnolent period.

LEVIN (1936) who had written extensively on the problems of narcolepsy, collected a number of similar cases who showed periodic somnolence associated with hunger from the literature (KLEINE, 1925, LEVIN, 1929, LEWIS, 1926, DANIELS, 1934, KAPLINSKY and SCHULMANN, 1935) where such cases had frequently been included in a general 'somnosis' group. Levin recalled the extensive evidence associating excessive hunger with cerebral lesions particularly of the frontal lobe (PAGET, 1897, FULTON, 1932) and attempted to correlate this with a Pavlovian concept of inhibition in hypothalamic/ frontal lobe centres. He noted motor unrest, and a range of psychiatric symptoms were frequently associated with the syndrome. Another finding was that transitory illnesses such as tonsilitis or influenza were mentioned at the start of the somnolent episodes.

Similar cases in which hypersomnia was associated with a disturbance of eating and some psychiatric symptoms such as confusion, irritability and retardation were described by HYLKEMA (1940), CRITCHLEY and HOFFMAN (1942). Critchley and Hoffman christened the syndrome 'the Kleine-Levin' syndrome. They considered the possibility of hyperinsulinism in/

/in their cases but found no supportive evidence. Electroencephalography failed to support the possibility of frontal lobe damage in their cases. A further two cases were described by RONALD (1946). Again 'influenza' preceeded the hypersomnia in one case and confusion was noted during the hypersomnia in the other case. Ronald was in favour of a lesion in the floor of the third ventricle as the probable explanation for the syndrome.

A similar illness following an acute febrile delirium was described in a boy of thirteen by GREWEL (1947), and PALMER (1950) described two cases, one of which was a man of 45 years of age.

The concept of this disorder was attacked by PAI (1950). He reviewed a number of cases of extended sleep seen in military personnel during and after the War. Physical investigations were negative and he considered that as a group these sleepers were immature and their adjustment inadequate. The hypersomnia was understandable in the light of the personality and the environmental stress and Pai criticized the speculations of Levin and Critchley on the cerebral basis for the hunger and implied that adequate psychiatric investigation would have been more appropriate in these cases.

Nevertheless, ROBINSON and McQUILLAN (1951) described a definite psychotic confused clinical picture in a soldier who suffered periods of hypersomnia and overeating.

An EEG was normal in this case.

GALLINEK (1954) described three cases in which hypersomnia was associated with depressive symptoms, very severe in one case and overeating. Low grade pyrexia and polydypsia was also noted. Gallinek was in favour of an organic frontal lobe/hypothalamic lesion rather than a psychological approach to the syndrome.

ROTH (1957) in his monograph records three cases in which hypersomnia was associated with alteration of appetite. Encephalitis and psychiatric disturbance also occurred. SMITH (1958) recorded the case of a man aged 56, whose sleep episodes lasted as long as 52 days. Appetite was not affected. Further cases were added by ZARATE (1957) and RAMONGUERA (1959).

CRITCHLEY (1962) made a determined effort to put the syndrome on a regular basis. He reviewed the existing cases and added eleven from his case records and the records of Queen's Square.

In these cases he made the point that appetite itself may not be increased but the patient find difficulty in stopping eating whenever food is available. Therefore he preferred megaphagia to bulimia as a description of the disorder. He discounted all the female cases described and raised doubts about the syndrome occurring for the first time in middle age, although he accepted Palmer's case - a man of 44 years. Precipitants or perhaps/

/perhaps aetiological agents to the disorder were frequently cited as influenza or some other trivial infection, injury and excessive alcohol intake prior to the illness, the frequency when the disorder was found in physically active men, noteably servicemen.

Vasomotor symptoms, sweating and flushing were often mentioned during the sleep, but the patients were rarely incontinent. Rousability was usually good so that feeding was easy despite the fact that some patients slept at their meals. Irritability and occasional aggressive behaviour was frequently noted on arising these sleepers, and the commonest psychiatric symptoms were confusion and dissociation. Negativism, motor unrest and hypermotility and derealization were also frequent complaints. Thought disorder accompanied by hallucinatory experience made a diagnosis of schizophrenia likely in some cases. A general disinhibition and an expansive euphoria were common symptoms which led to management difficulties. At the end of the episode, a depressive anorexic picture with insomnia was frequent.

Physical examination showed evidence of pyramidal dysfunction in some cases, but the cerebrospinal fluid was usually normal. Electroencephalograph frequently showed evidence of cerebral hysfunction - patchy slow activity rarely well localized.

During the 'sleep' itself, electroencephalograms were taken fnfrequently and in one of Critchley's cases/

/cases continued to show relaxed drowsy rhythms - alpha activity in patches and a little intermediate slow activity. Air encephalography in some cases showed evidence of minor abnormalities only.

Critchley considered that all the female cases of the disorder up to that time, 1962, showed some atypical features and he therefore decided to limit the syndrome to a disorder of adolescent or young males and saw it as a recurrent symptom complex which appeared over a period of years in the life of the individual, but ultimately disappeared so that the long term prognosis was good. On the whole Critchley saw this as a disorder of cerebral function of unknown aetiology rather than a primarily psychiatric disease.

A very full account of a female patient who had suffered from a phasic illness since the age of twenty - eighteen years previously, was given by GILBERT (1964). This patient showed a cycle of active behaviour succeeded by a phase of depressed and hostile feelings leading to a period of hypersomnia and overeating. The elated and depressive phases were prominant but a diagnosis of manic depressive disease not thought proven. Detailed investigation showed the unsuspected finding of a low normal intelligence level (Full scale IQ 78.) and raised corticosteroid excretion. Electroencephalogram was normal and showed evidence of sleep changes during the hypersomnia. GILBERT was in favour of "diencephalic dysfunction" basis for the syndrome.

A further female case which fulfilled the other criteria laid down by Critchley, was described by Earle (1965). Detailed psychiatric assessment impressed the author with the 'manic-depressive' qualities of the syndrome and the immaturity and lack of identity of the patient herself. Nevertheless he felt that the disorder was more in keeping with a hypothalamic disorder than a primarily psychiatric illness.

GARLAND (1965) in a very striking description of a case came out strongly for Critchley's 'organic' concept of the syndrome. His case, a man of 21 years showed clear evidence of a diminhibited sexually active disorganized state with marked overeating and complaints of hunger. He was inert for long periods but Garland was doubtful of the question of sleep preferring to consider this inert state as one of withdrawal. Investigation was unhelpful although minor abnormalities were found on air encephalography. The disorder remitted spontaneously and was thought of more in terms of a diencephalic dysfunction than a psychiatric disorder.

The Kleine-Levin syndrome is rather a tenuous concept. Experience does not allow Critchley's limitation of the syndrome to male adolescents to survive and the age span increases as female cases of the syndrome are added. Most authors are struck with the 'organic' aspects of the illness although investigations rarely support this and give/

/give unequivocal evidence of cerebral pathology. Equally opinions are divided on the main symptoms of the syndrome - whether 'sleep' is the right term for the inactive unresponsive state, and whether the overeating is associated with hunger or not. The confused hallucinatory mental state is reminiscent of a 'periodic psychosis' as described by LEONHARD (1961). In particular it is noticeable in reviewing the literature that very little attention has been paid to the study of sleep in these hypersomniacs.

The Kleine-Levin syndrome appears to fade away at the edges into states of hypersomnia some of whom can be seen to be hysterical (PAI 1950) and as a defense in a situation where the individual was incapable of dealing with hostile emotion (GOLDSTEIN, 1958). Hypersomnia in association with the menstrual cycle (KLEINE, 1925; ROTH, 1957) at the menarche (WENZEL, 1960; JOCHIMS, 1963) hypersomnia related to depressive illness in some patients (MICHAELIS, 1964) all merge with the organic syndromes in which hypersomnia is a symptom (KLEITMANN, 1963). Cases described under the heading of Kleine-Levin syndromes may subsequently be removed to another category. For example the case described by ROSENKOTTER (1955) as example of the Kleine-Levin syndrome was subsequently found to have suffered from encephalitis. A case described by ZARATE (1957) suffered from classical cataplexy and sleep attacks and was considered/

/considered narcoleptic. So it is difficult to find criteria which will satisfactorily delineate the Kleine-Levin syndrome from other forms of hypersomnia.

A symptom common to both narcoleptic and to the Kleine-Levin syndrome is obesity and this forms a link with another class of hypersomnia.

3. The Pickwickian Syndrome

This approach arose not on account of the hypersomnia, but because of interest in the effects of enlargement of the abdomen upon respiratory function. The work of CUGELL (1953) in pregnancy and ABELMAN (1954) in ascites, showed that regardless of the actual cause, increasing girth led to a decrease in respiratory reserve and eventually to relative ventilatory failure. Carrying this argument further SIEKER (1955) reported on four patients with extreme obesity who showed somnolence, periodic respiration, intermittent cyanosis, polycythaemia and right axis deviation. Ventilatory studies showed decreased total lung volume, decreased functional reserve capacity and decreased expiratory reserve volume. To the syndrome they gave the term 'obesity heart disease', and the syndrome appeared to be reversed by loss of weight. In 1955 also Auchincloss reported on a similar case in whom a weight loss of 24 lbs and repeated phebotomi diminished the dyspnoea and oedema symptoms, but not the alveolar hypoventilation syndrome itself. WEIL (1955) reported on two cases of polycythaemia/

/polycythaemia and obesity and found that weight reduction was associated with a fall in the R.B.C. count.

BURWELL (1956) initiated the interest of sleep workers in the syndrome by placing emphasis on the somnolence and christening the disorder the 'Pickwickian Syndrome'after the boy 'Joe' in the Posthumous Papers of the Pickwick Club (DICKENS, 1835). The patient in this report (BURWELL, 1956) did in fact complain of short lived episodes of sleep but although he reported occasional syncope no episodes of cataplexy occurred. Obesity was marked and cyanosis, severe somnolence twitching movements while asleep, and irregular respiration were prominent symptoms and signs. Apnoea with intervals of tachypnea rather than hyperpnea were observed. Right-sided cardiac failure was evident, but neurological and electroencephalography were normal. Hypoxia and a raised carbon dioxide level were found at rest, and it was found that the respiratory centre was less sensitive to Co_2 than normal. Weight loss was associated with improvement in the blood gases, respiration function and general state of the circulation but the authors are reticent as to the effect of weight loss on the somnolence. However, the argument that severe obesity leading to ineffective respiration, decreased sensitivity of the respiratory centre to CO_2 and polycythaemia was supported by this work and it seemed acceptable that the somnolence was associated with the anoxia and hypercapnia. While/

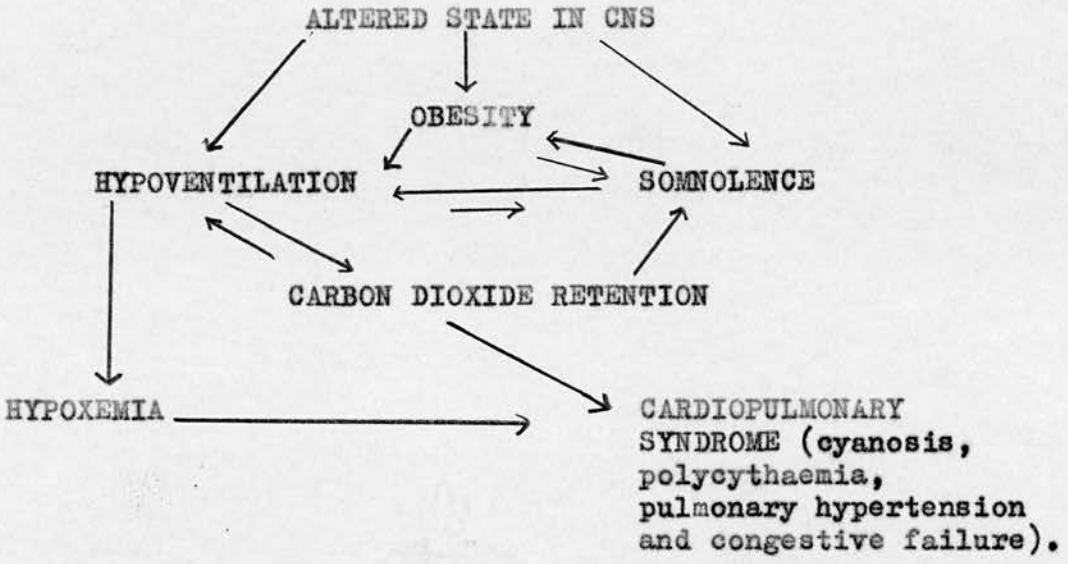
/While the peripheral causation of the syndrome gained acceptance in several investigations (HACKNEY, 1959; GERARDY, 1960), investigations in normal subjects and narcoleptic patients (BIRCHFIELD, 1958, 1959, SIEKER, 1960, ROBIN, 1958) showed that sleep was itself associated with a rise in CO_2 levels and a slight fall in oxygen tension and with reduced sensitivity of the respiratory centre to CO_2. Narcoleptics showed slight hypercapnia and anoxia at rest which was in keeping with a chronic and mild drowsy state. (BULOW, 1963).

Reports of hypoventilation effects due to a 'central' process were made in cases of barbiturate intoxication (WILSON, 1954), dystrophica myotonia (KILBURN, 1959) and encephalitis (EFRON, 1957; GARLAND, 1958) which were similarly associated with chronic somnolence, and it was suggested that a 'primary' hypoventilation syndrome due to medullary brain damage may produce somnolence (RODMAN, 1959).

Sieker suggested in 1960 that as narcoleptics frequently showed symptoms in common with the Pickwickian syndrome - hypoventilation, obesity, periodic respiration, it might be that both 'central' and 'peripheral' factors played a part in the production of the syndrome of hypoventilation.

His schema was:-/

His schema was:-



On the basis of this schema, weight reduction would affect the cardiopulmonary and ventilating components but not necessarily relieve the somnolent symptoms.

DRACHMAN and GUMNIT (1962) therefore directed their investigation towards the somnolent aspects of the Pickwickian syndrome. The ventilating aspects of the state were in keeping with BURWELL (1956) and there was great improvement with weight reduction. Simultaneous monitoring of electroencephalograph, respirations and oxygen tension were carried out, and were shown to vary in a series of cycles. The EEG at rest showed an altered record giving way to drowsiness and then to abrupt waking. In keeping with this oxygen tension was lowered and CO_2 tension raised. Breathing effectively restored the oxygen tension and this was followed by a period of apnea which was associated/

/associated with drowsiness. As O_2 tension fell further arousal occurred and effective respiration restored the oxygen tension.

It was thought that the hypersapnia resulted in reduced sensitivity of the respiratory centre so that the control of respiration was more dependant on carotid and aortic body receptors - less sensitive to oxygen tension. Drachman and Gumnit showed that rebreathing 70% oxygen resulted in apnea. Increasing anoxia resulted in arousal via the carotid body chemo receptors which 'overshot' the mark as far as ventilation was concerned so that the correction of oxygen tension allowed sleep to return. Marked weight loss correcting the hypoventilation and hypcapnia was found to improve the state of recurring somnolence in their patient greatly, and muscle twitching ceased.

The association of somnolence with hypoventilation was explored further by JUNG and KUHLO (1965) who for the first time recorded the over-night sleep of Pickwickian patients. The Pickwickian patients slept very badly. Sleep was associated with apnea and ineffective jerking respiratory movements. Anpea might last 40 sec and was associated with cyanosis. Arousal with some violent snorting respirations then occurred. This respiratory cycle interrupted the normal cycles of sleep so that the patient rarely succeeded in descending far down a slow sleep cycle. (Usually only to Stage II or transitorily to Stage III).

They suggested that sleep was associated with a respiratory block as the upper pharynx was atonic in sleep, but raising the jaw and tongue manually did not remove the apnea. pCO_2 was shown to be high during sleep, and apparently ineffective as a respiratory stimulant. (GERARDY, 1960). REM sleep was considerably depressed and was noted only after weight reduction had taken place. The authors noted that in REM sleep, although they in fact recorded very little, there were no apnaic periods and respiratory was regular. The involuntary and sometime myoclonic jerks of the Pickwickian occurred towards the end of the apnaic period and were thought to be part of the 'arousal' mechanism due to chemoceptor stimulation or the direct effect of CO_2 tension on the reticular formation.

Thus the original concept of the Pickwickian syndrome as 'peripheral' disorder based on the effects of obesity on respiration which seemed entirely satisfactory initially, did not entirely explain the findings in all patients or in narcoleptics and increasingly the efficiency of the respiration centre was questioned so that some 'central' deficiency was postulated.

VI. Treatment

Exercises, diet and sunlight were recommended by ARETAEUS for the treatment of 'Lethargics' but apart from purging and blood WILLIS recommended an extract of coffee in 1672. This seems to be the first drug recommended for the treatment of somnolence.

DANA (1994) reviewed treatment in the nineteenth century. Noises to arouse the patient, blisters, cupping and rubefacients. Sternutatorics, castor, emetics and purges were used. Hydrotherapy electricity, general hygeenic measures and tonics also. Symptomatic treatment with coffee, caffein, coca, belladonna nitrite of amyl and sternutatories -of powdered cinecliona and white hellebore, had all been used.

On the whole there were few supporters of the use of sedatives, but surgery was occasionally used in the form of an exploratory burr hole (BROWN, 1907, Carlill, 1919).

The withdrawal of cerebrospinal fluid (LHERMITTE and NICHOLAS, 1924) and the removal of C.S.F. with the replacement of air was advanced by Lhermitte 'to modify the functional or dynamic state of the negative centres' in the floor of the third ventricle. REDLICH (1931) was unconvinced of the usefulness of this treatment. Injections of small quantities of air into the cisterna magna were used by BENEDEK and THURZO (1931) with good immediate results, and DANIELS (1934) found that lumbar puncture was helpful in a case of post traumatic narcolepsy.

DOYLE and DANIELS (1932) treated nine patients with irradiation of the hypothalamic area without much evidence of benefit and one died within days of treatment. They and CAVE (1931) attributed this to softening in a neoplastic growth but no pathological findings were described.

Attempts to increase the amount of overnight sleep in order to reduce the need for sleep attacks in the day by prescribing hypnotics were unsuccessful and DANIELS (1934) reported indifferent results with oral caffeine. Thyroid extract was used by REDLICH (1931) which improved the symptoms of three of the twenty patients treated. Pituitary extract was similarly used by BEYERMANN (1930) and RATHNER (1929). A ketogenic diet was said to have helped one patient of SOLOMAN's (1930).

Caffeine was succeeded by Ephedrine sulphate first used by JANOTA (1930), and this drug was hailed by DOYLE and DANIELS (1932) as the first effective treatment of narcolepsy. The regime was 25mg of drug before breakfast and before lunch and DANIELS (1934) was satisfied that the drug was reasonably effective in producing relief of symptoms and also concluded that cataplexy was more amenable to ephedrine treatment than sleep attacks or drowsiness were.

Amphetamine was used as benzedrine by PRINTZMETAL and BLOOMBERG (1935) and generally accepted as a specific treatment for narcolepsy. Printzmetal discovered that the drug produced insomnia in normal people and therefore chose/

/chose narcolepsy deliberately as the disorder of choice to test the stimulating effects of the drug. A blind trial proved that benzedrine was approximately three times as effective as ephedrine.

Ciriously early data convinced clinicians that amphetamines did not have tolerance or addiction problems and were low in toxicity (MURPHY, 1940). It was therefore incorporated into the text books of medicine of the period as the logical treatment (NOYES, 1948, REESE, 1943).

The possibility that amphetamine contributed to a paranoid psychosis was raised by YOUNG and SCOVILLE (1938) but largely dismissed by other authors. (DRAKE, 1949). However the increasing awareness of the addicting problem and the induction of paranoid symptoms which became apparent in the 1948-51 period (SCHNEUCH, 1948, O'FLANAGAN, 1950, MONROE, 1947, NORMAN, 1945, WALLIS, 1949) made the need for a replacement much clearer.

Methyl phenidate was used first on the treatment of narcolepsy by YOSS and DALY (1956). Methyl phenidate (Ritalin) had been found to antagonize the sedative effects of phenobarbital (DRASSO and SCHMIDT, 1954) and was a logical choice in the treatment of narcolepsy. Yoss and Daly's initial survey and a more complete evaluation (1959) were in favour of the drug. It was considered by these authors to be the drug of choice and later papers endorse this recommendation, (SIEKER, 1960).

AKIMOTO (1960) studied the effects of a number of drugs in varying doses - sufficient to abolish the sleep attacks, or the cataplexy in a given patient for a set time. Methyl phenidate was again found to be effective, and several amphetamine derivatives were also found to prevent sleep attacks and cataplexy. On an empirical basis, antidepressant drugs were assessed and imipramine was found to have marked anti cataplectic effects while a hydrazine mono-amine oxidase inhibitor (Catran) was ineffective.

Another approach worthy of concern, was that of DYNES, (1943) who seeing the possibility of a connection between the weakness of cataplexy and the weakness of familial periodic paralysis, prescribed potassium salts for narcolepsy and showed that it was an effective measure against cataplexy but had no effect on sleep attacks themselves. Although, in the past 30 years a large number of drugs have been used to treat narcolepsy, amphetamine and its derivatives replaced by methyl phenidate to some extent, remains the standard by which all the other therapeutic measures are examined. Imipramine has achieved fairly wide acceptance as an effective drug in treating cataplexy.

Subjects and Methods

Supply of patients

From 1st January, 1965 by courtesy of several neurological and psychiatric consultants in the region, patients referred to neurological clinics at the Northern General Hospital and Edinburgh Royal Infirmary for investigation of hypersomnia in any form were asked if they would take part in a research programme into this group of disorders. All were agreeable with one exception who was in fact treated initially for a psychotic illness and later co-operated in the study.

At a suitable time, patients were invited to visit the Sleep Laboratory at the Department of Psychiatry and the method of recording sleep was explained in detail.

A standard interview, designed to investigate the various aspects of hypersomnia was then administered and followed by a routine psychiatric assessment.

Standard investigations - a full blood examination, protein bound iodine estimation, skull and chest X-rays and a lumbar puncture, had usually been carried out as part of the neurological investigation, and a routine clinical encephalogram was frequently performed as an outpatient. At this first interview gaps in these investigations were noted and the investigation ordered.

Arrangements were then made to record an overnight sleep in the week following the first interview.

A number of patients were referred in the same way from psychiatric colleagues, and I was also able to interview a number of patients in hospital when admitted for investigation of hypersomnia or associated symptoms.

Finally after I had taken part in a B.B.C. programme on sleep and discussed the problem of narcolepsy with a narcoleptic patient, a number of people wrote and asked for investigation of their hypersomnia complaints. In all cases they were advised to discuss the problem with their general practitioner, but a number of doctors subsequently wrote requesting that their patient should be investigated.

Sleep studies and associated tests

The technique for recording both nocturnal and diurnal sleep was identical. After changing into comfortable clothes patients had silver disc electrodes attached to face and submental region with adhesive strapping, and to the scalp with collodian. Electrodes routinely occupied outer canthus and frontal boss situations, around the eyes, and were placed over the belly of the submental muscle group on either side. Scalp electrodes were placed in the midline in positions intermediate between C_z and P_z, and P_z and O_z positions of the 10-20 system (JASPERS, 1958). Long cables (approximately 6-8 feet) from each electrode were formed into a cord which was plugged into an adjacent headboard, affording a considerable range of subject movement whether in bed or in a chair. Bipolar montages were switched/

A SUBJECT WITH ELECTRODES IN PLACE. LEADS ARE GATHERED IN ONE CORD AND ALLOW A GREAT AMOUNT OF MOVEMENT IN BED.

/switched to record eye movements, electroencephalogram and muscle tone on an encephalograph (Ediswan, 8 channel; Alvar Reega 14 channel). The EEG machine routinely ran at 15 mm/sec., throughout the night consuming approximately 0.25 mile of paper. EEG.

Diurnal sleep records were obtained from each patient usually on three or more occasions. The subject was asked to attend at the Laboratory at 12 noon where electrodes were put on, a process of approximately 20 minutes duration.

Patients had been asked to avoid all situations conducive to sleep during the course of the morning, and to be as active as possible. Blood was taken off at this time for glucose estimations and usually this left a lull period of up to 40 minutes before lunch was served. Left to themselves, to read but not to talk to the experimenter who remained in an adjacent room throughout, most subjects slept promptly.

Their sleep was recorded until either the nurse arrived with the patient's lunch or the patient woke spontaneously. All patients were asked to record on arousal any mental activity which they recalled during this period.

A number of diurnal episodes of sleep were recorded at other points in the day - frequently in the late afternoon or early evening, (1600 - 2000). If the patient complained of prolonged sleep, the overnight recording was extended into the following morning on a number of occasions.

On one occasion some 36 hours of sleep was recorded continuously.

A variant of the techniques used to record diurnal sleep was the use of a 14 yard cable extension which offered a much greater freedom of movement. Records with the subject standing offered the possibility of recording cataplexy.

Overnight studies

The first night recorded in a laboratory is usually found to be atypical (MENDELS and HAWKINS, 1957), and such records are considered spparately in the results section. However they served to familiarize the patient with the technique. Usually 3 or 4 overnight records were arranged to be taken at intervals over the next 4-5 weeks. During the series the opportunity to wake the subject from REM sleep or from slow wave sleep in the morning was utilised to record mental activity.

In some patients with hypersomnia complaints, serial blood samples were taken during the night for glucose estimation.

The Pickwickian patients were also recorded visually via closed circuit television and the use of videotape recorders so that their respirations could be followed closely. Following this they were admitted to the Department of Medicine, Royal Infirmary, Edinburgh where a catheter was placed in the radial artery so that/

/that ventilatory responses and serial blood gas estimations could be made overnight.

Control Group

The first 15 patients suffering from idiopathic narcolepsy (8 female, 7 male) were considered as a separate group and control subjects matched for sex and approximate age obtained from staff and student populations were recorded both overnight and for pre and post prandial naps.

Drug Study

1. Tryptophan load

Work in this laboratory (OSWALD, 1965) had shown that an oral dose (5G) of laevo tryptophan given immediately prior to sleep, had in certain individuals the effect of enhancing the "pressure" for REM sleep, i.e. it brought the first REM sleep period forward so that the delay to first REM sleep from the start of sleep (D) was below the lower normal limit of 45 minutes. Short latency for REM sleep was also noted in drug withdrawal studies (OSWALD, 1965) and found to be associated with very intense dream activity. Further it was found that this effect of tryptophan was blocked by prior treatment with a drug considered to be a serotonin (5HT?) antagonist (methysergide, Deseril).

A number of overnight records was carried out with each of the 15 narcoleptic patients after ingestion of 5G laevo tryptophan. In a smaller group of these patients the effects of methysergide administration prior to a tryptophan load/

/load was also studied.

Effect of sympathetico mimetic drugs

In a number of instances, the subject on referral had already received amphetamine or methylphenidate. Some patients were happy to stop the drug and they were recorded at night over the withdrawal period. Tryptophan loading tests were carried out when the patients were taking amphetamine or methylphenidate and after the drugs were withdrawn.

Other patients wished to continue the drugs while sleep studies were carried out and their response to tryptophan loads were studied while on drugs.

Also the opportunity to start patients on a number of drugs - amphetamine, methyl phenidate and imipramine and mono-amine oxidase inhibitors, was utilized to follow the responses to tryptophan loads.

The studies involved considerable contact with patients suffering from narcolepsy and other syndromes of hypersomnia and afforded much insight into their problems. This material is utilized further in the discussion of the results of these studies.

RESULTS

Part 1: Clinical Studies

1. Total patients seen = 54.

2. Diagnosis (made at time of first referral).

		Male	Female	Total
A	Narcolepsy. Idiopathic	16 (53%)	14 (47%)	30
	Symptomatic	4	2	6
B	Idiopathic Hypersomnia	7	6	13
C	Pickwickian Syndrome	2	0	2
D	Kleine Levin Syndrome	2	1	3
	Total patients	31 57%	23 43%	54

Idiopathic Narcolepsy Group n = 30.

1. Distribution of Symptoms in the Narcolepsy Group

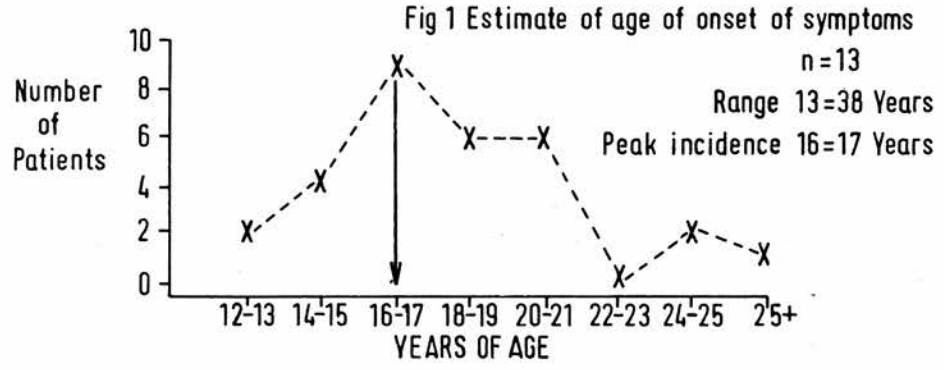
	Idiopathic	Symptomatic
Sleep attacks + cataplexy	11	2
Sleep attacks alone	2	4
SA + C + Hypnogogic hallucinations	0	0
SA + C + Sleep paralysis	10	0
Full tetrad	7	0
SA + SP + HH	0	0
SP	0	0
C	0	0
Total	30	6

2. Comparison of symptom combinations of narcoleptic tetrad (Yoss and Daly, 1957) with series of Sours (1963).

	Present study	Sours (1963)
n	36	75
Sleep attacks alone	17%	19%
SA + another symptom	100%	96%
Cataplexy	83%	72%
Sleep paralysis alone	0%	4%
SP with another symptom	42%	27%
Hypnogogic hallucinations	19%	28%
Full tetrad	19%	11%

3. Estimate of age at first symptom developed

F I G U R E I



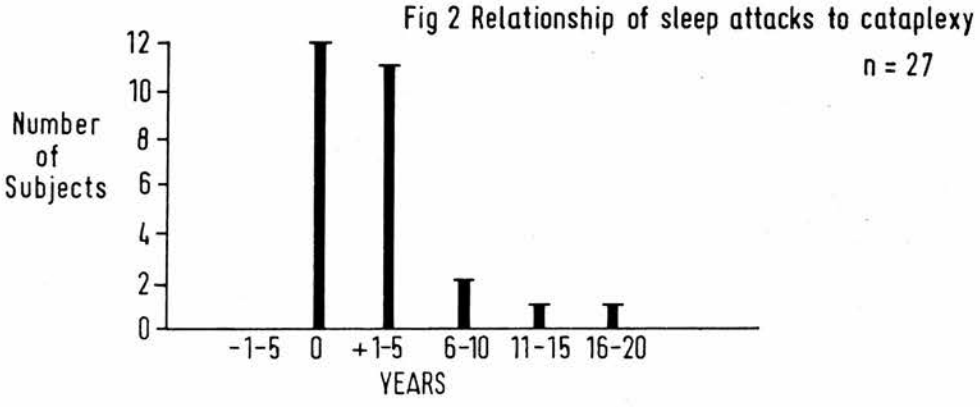


FIG. 1. AGE OF ONSET OF SYMPTOMS OF NARCOLEPSY

FIG. 2. RELATIONSHIP OF ATTACKS OF CATAPLEXY TO ONSET OF SLEEP ATTACKS

4. Relationship of the onset of sleep attacks with the onset of cataplexy.

F I G U R E II

5. Family History

A family history of hypersomnia symptoms was recorded in 10 patients. Prolonged sleep episodes were noted in the relatives of 3 patients. Sleep attacks were described in six relations of six patients. Sleep attacks and cataplexy was recorded in the sister of a female patient.

6. Duration of symptoms

F I G U R E III

7. State of the disorder

	Male	Female	
n = 54	%	%	%
Improvement	5.6	3.8	9.4
Static	28.7	18.8	47.5
Fluctuant	9.8	11.0	20.8
Deterioration	12.5	9.8	22.3

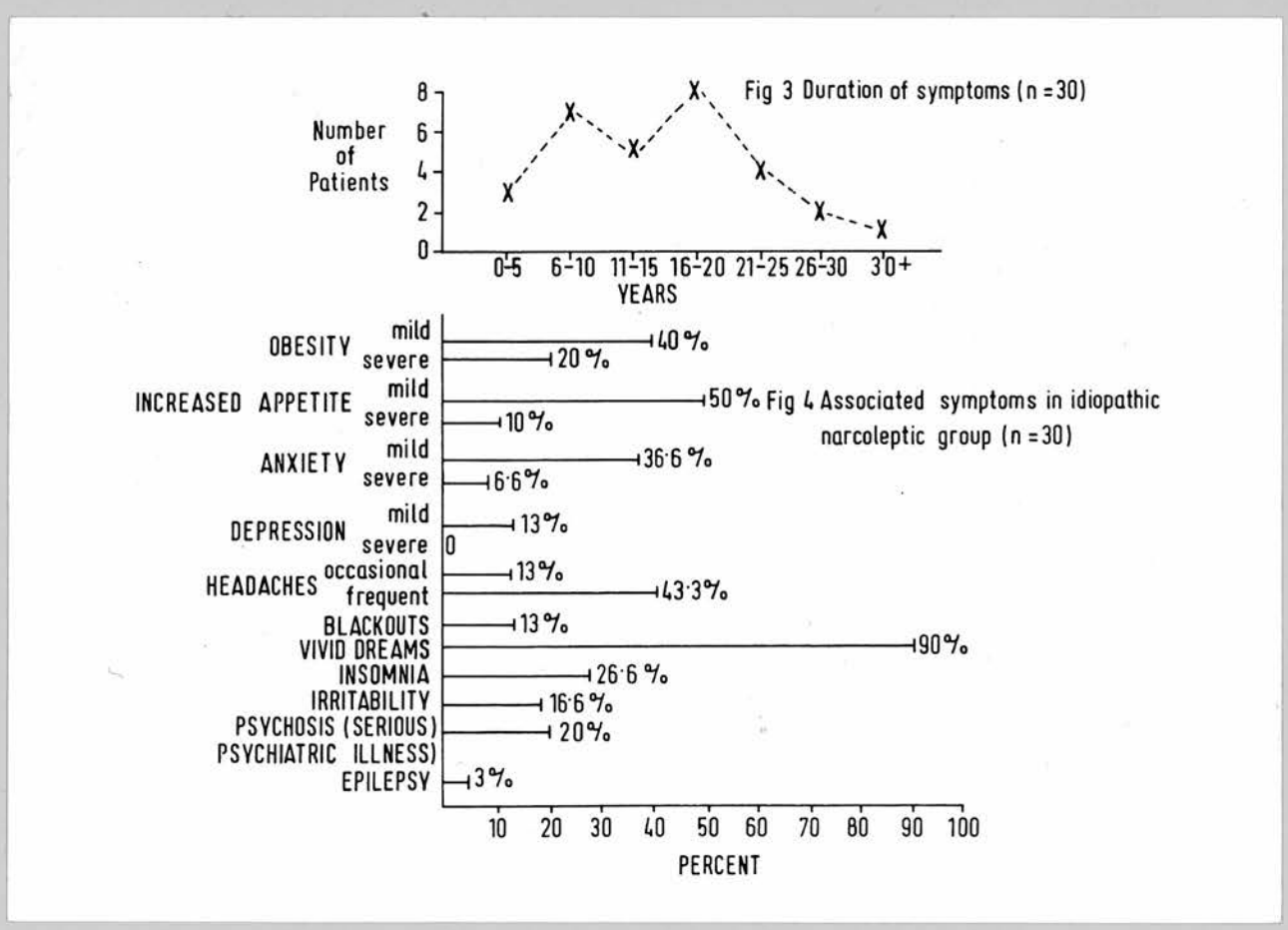


FIG. 3. DURATION OF NARCOLEPTIC SYMPTOMS

FIG. 4. THE INCIDENCE OF ASSOCIATED SYMPTOMS IN NARCOLEPTIC PATIENTS

8. CATAPLEXY:

Incidence	27 cases	84% of total group
Type:-		
Partial i.e. involving face or arm and leg	27	100%
Total - involving a 'drop'	8	29.6%
Evoked by:-		
Laughter	23	85%
Aggression or anger	11	41%
Physical exercise (running or in course of game, i.e. tennis)	3	11%
Excitement	5	19%
Dysarthia and aphonia with excitement	6	20%

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9. SLEEP PARALYSIS:

Described in 16 cases (44%). 9 Male. 7 Female.

All cases were predormital.

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10. HYPNOGOGIC HALLUCINATIONS:

Described in 7 cases (19%) - i.e. only those with full tetrad of narcolepsy. Never described by other patients. Frequently visual and often vivid and frightening. Tactile hallucinations - hands touching face or other parts of body also mentioned. Most patients had great difficulty in distinguishing between hypnogogic hallucinations and vivid dreams, and it was often difficult to decide whether the episodes of hallucination had been hypnogogic or hypnopompic although on some occasions the hallucinatory experience coincided with sleep paralysis at the beginning of sleep.

11. Associated symptoms (in group of idiopathic narcolepsy - = 30).

F I G U R E IV

12. Possible aetiological factors.

A	Head injury	Sufficient to produce loss of consciousness described in 7 cases (23%).
B	Meningitis	0.
C	Encephalitis	3 cases. Each diagnosis depending entirely on a patient's description of a prolonged influenzal illness prior to first narcoleptic symptoms.
D	Venereal Disease	4 cases described urethral discharges. Gonorrhea or non specific urethritis. No case of syphilis,

13. Psychiatric disorders

Overall incidence 76.6%.

A. Psychoses:

Severe paranoid hallucinatory illness	3 cases (10%)
Considered schizophrenic	1 case
Considered hypomanic	1 case

B. Affective states or personality disorders:

Schizoid personality	2 cases (6%)
Hypomanic personality	2 cases (6%)
Hysterical personality	1 case (3%)
Obsessional personality	2 cases (6%)
Aggressive/psychopathic personality traits	4 cases (12%)
Vague, ineffectual drifting "inadequate personality"	7 cases (23%)

14. Existing treatment

Amphetamine	14 cases (46%)
Methylphenidate	7 cases (23%)
Thyroid extract	1 case (3%)
Phenobarbitone	3 cases (10%)

15. Other possible precipitating causes

Menarche	3 cases (10%)
Prior to important school examinations	10 cases (30%)

16. Routine investigations

A. Protein bound iodine estimation. All determinations were within the normal range for this laboratory. (3-8 uG/100 ml).

Mean 5.36 uG/100 ml.

Range 3.8 - 7.2 uG/100 ml.

B. Skull X-ray. No abnormalities found in this group. No evidence of old healed fractures. Sella turcia was considered normal.

C. Lumbar puncture failed to show any definite abnormalities in this group of patients.

D. Haematological investigations. Blood picture and erythrocyte sedementation rates were normal.

Haemocrit estimations. Haemoglobin (G/100 ml) was within the normal range. Mean values 14.6 (male) 13.2 (female). Overall mean 13.9G%.

E. Glucose estimates at the start of the diurnal sleep.

Mean 79.83 mg/100ml.

S.D. 9.0595 mg/100ml.

Range 61.90 mg/100ml.

Within normal range.

Symptomatic Narcoleptics

n = 6.

I. Distribution: 4 male, 2 female.

II. Aetiological factors.

i) Encephalitis (proven illness documented with hospital notes and lumbar puncture abnormalities) 2 cases

ii) Head injury (documented hospital records. Prolonged unconsciousness and retrograde amnesia). 2 cases

iii) Carbon monoxide poisoning (documented hospital notes. Prolonged coma with extra pyramidal abnormalities during recovery). 1 case

iv) Cerebral tumour. (Carcinoma of breast with multiple secondary deposits and evidence of cerebral metastases). 1 case

III. Symptoms. n = 6.

Sleep attacks	6 cases	(100%)
Cataplexy	2 cases	(30%)
Persistent drowsiness		(100%)

No account of sleep paralysis or hypnogogic hallucinations. No patient had full narcoleptic tetrad of symptoms. Prolonged sleep (over 24 hours) was reported in 2 cases (30%), and extended overnight sleep in 5 cases (83%).

IV. Family history - none.

V. Treatment.

One patient had received amphetamine and methylphenidate (Ritalin) at times. Another receiving phenobarbitone.

VI. Associated symptoms.

Obesity present in 2 cases (30%).

Appetite was increased in both cases.

Depression was complained of by 2 patients (30%).

Anxiety symptoms were present in 3 cases (50%).

All patients complained of headache.

'Blackouts' were noted by 3 patients (50%).

Vivid dreams were noted by one patient and insomnia was complained of by another patient.

Irritability was a persistent complaint (5 cases, 83%).

VII. Duration of symptoms. Range 1-40 years.

VIII. Investigations.

a) Protein bound iodine estimates normal in all cases Range 3.8 - 5.6 uG/100ml.

b) Skull X-rays confirmed the loss of frontal bone in one case and the basal fractures in the other case of head injury but were otherwise normal.

c) Lumbar puncture. This was within normal limits except in moderately raised protein levels in Case III and Case IV.

d) Haemocrit estimations. Within normal range. Range 13.6 - 14.6 G/100ml.

e) Blood glucose estimates at time of diurnal sleep.
Mean 76.1666 mg/100ml.
S.D. 8.9087 mg/100ml.
Range 70-91 mg/100ml.

Within normal limits.

Idiopathic Hypersomnia

1. Number of cases - 13.

2. Distribution. 7 male, 6 female.

3. Age distribution. 6-59 years. Average age - 29. Peak age of incidence - 20.

4. Symptomatology.

Prolonged drowsiness	11 cases (85%)
Sleep attacks	9 cases (69%)
Cataplexy	0 cases
Prolonged sleep (24 hours +)	9 cases (69%)
Extended overnight sleep	12 cases (92%)
Hypnogogic hallucinations	
occasional	4 cases (31%)
regular	0 cases
Sleep paralysis	0 cases

General picture of the syndrome is overall drowsiness extending to sleep attacks in the day and prolonged overnight sleep, with more prolonged periods of sleep occasionally.

5. Family History.

A positive history of sleep disturbance was obtained in 4 cases (31%).

Three relatives (2 fathers and 1 sister of patient) were said to have episodes of prolonged sleep at some period of their lives (usually adolescence or young adult periods). One father was said to suffer from sleep attacks.

6. Aetiological factors.

Meningitis in one patient.

Head injury was recorded on only one case.

No cases of venereal diseas was found.

No evidence of a connection of the sleep disorder with puberty was discovered.

7. Duration of symptoms.

Range was found to be very wide - 1 to 39 years.

Symptoms had been present for:-

1- 5 years in 5 cases (46%)

6-10 years in 5 cases (46%)

over 20 years in 3 cases (23%)

8. Treatment.

3 patients had received amphetamine and one was receiving methylphenidate.

9. Associated symptoms.

Obesity	5 cases (46%)
'Blackouts'	1 case (7%)
Appetite increase	5 cases (46%)
Irritability	0 cases

Anxiety symptoms	5 cases (46%)
Psychiatric disorders (other)	5 cases (46%)
Headaches	7 cases (54%)
Vivid dreams	0 cases
Insomnia	1 case (7%)

9. Investigations.

a) Protein bound iodine estimates.

Mean	6.7 uG/100ml.
Range	2.6 to 6.8 uG/100ml.

Within normal range.

b) Skull X-rays. No abnormalities noted. Sella turcia normal.

c) Lumbar puncture. No significant abnormalities.

d) Haemocrit estimates.

Mean	13.6 uG/100ml.
Range	12.1 to 14.8 uG/100ml.

e) Blood glucose estimation at onset of diurnal sleep.

Mean	78.5384 mg %
S.D.	7.5455 mg %
Rante	70 - 91 mg %

10. Nocturnal blood glucose estimates.

<u>Subject M2</u>

Sample	I	22.00	Awake	81 mg %
	II	22.30	Awake (in bed)	77 mg %
	III	23.00	Stage I SWS	91 mg %
	IV	23.40	Stage IV SWS	92 mg %
	V	00.10	REM sleep	86 mg %
	VI	01.00	Stage II SWS	82 mg %
	VII	02.00	Stage IV SWS	80 mg %
	VIII	03.00	Stage REM	82 mg %
	IX	04.00	Stage II	76 mg %
	X	05.00	Stage REM	80 mg %

XI	06.00	Stage III	78 mg %
XII	06.15	REM sleep	82 mg %
XIII	07.00	Stage II	84 mg %
XIV	08.00	Awake from REM	92 mg %

Subject M3.

Sample				
	I	22.30	Awake	96 mg %
	II	22.50	Awake (in bed)	90 mg %
	III	23.30	Stage II SWS	86 mg %
	IV	24.00	Stage IV SWS	86 mg %
	V	01.00	Stage III SWS	80 mg %
	VI	02.00	Stage REM	84 mg %
	VII	03.00	Stage II SWS	86 mg %
	VIII	04.00	Stage III SWS	80 mg %
	IX	05.00	Stage II SWS	76 mg %
	X	06.00	Stage REM	80 mg %
	XI	07.00	Stage II	86 mg %
	XII	08.00	Stage I/Awake	88 mg %

11. Psychiatric Assessment.

Three categories of psychiatric disorder occurred within the group of idiopathic hypersomnia.

1. Addiction to drugs - 3 cases. One patient was addicted to meprobamate (Equanil) (FV). One to Librium (MVI) and a third was abusing barbiturates (FVI). The first two patients were admitted to hospital for investigation of increased somnolence. FV (meprobamate addict) developed a withdrawal delirium with epileptic fits while under investigation. MVI was found to have taken an overdose of Librium which had precipitated his admission to hospital in a prolonged drowsy state. FVI was admitted to hospital because of an epileptic fit which was associated with an effort on her part to stop the drug (Sodium amylobarbitone).

2. Definitive psychiatric illness.

   Depressive illness - 1 case
   Hysterical personality disorder - 1 case
   Schizoid personality - 1 case.

3) A syndrome particularly prevalent in this group was one of uninvolvement and general apathy with gross over dependence on parent figures. No psychotic symptoms emerged although the disorder was predominantly a 'loss of volition'. Present in 5 cases (46%).

4) Other disorders.

One patient (FII) was found to have severe marital difficulties and financial difficulties which she was coping with by obtaining 3 jobs, an office cleaning job in the early morning, followed by a Gallop poll interviewer post which entailed travelling extensively in the day, and in the evening she worked as an assistant to a Veterinary surgeon taking saliva samples from greyhounds in a local track (a job she had done before marriage). She complained of sleep attacks while travelling in the day but was in fact suffering from chronic moderately severe sleep deprivation as she had an average 3-4 hour sleep a night. About two years later she was admitted to a psychiatric hospital for treatment of a depressive illness.

Another patient (FV) was in severe marital difficulties with attendant sexual problems. She took a job as a night nurse, did housework when she returned home in the morning (after husband had left) and slept the remainder of the day until she had to go to work. On rest days she slept almost all the available time spent at home, complained of persistent sleepiness and sleep attacks while on duty at night. She had in fact engineered a marital separation in that no contact existed between husband and wife.

<u>Patients originally diagnosed to suffer from Kleine Levin Syndrome</u> n = 3.

1. Distribution - 1 female, 2 male. Ages: Female 19. Male 27 and 29.

2. Complaints.

Drowsiness -	intermittent	1 case
	persistent	2 cases

Sleep attacks) Cataplexy)	0 cases
Prolonged sleep episodes of 3-4 days	3 cases
Extended overnight sleep	3 cases

3. Duration of symptoms. Range 3-15 years.

Onset of sleep disturbance was at 14-16 age period in all cases. Pattern of symptoms - disorder was of episodes of hypersomnia lasting several days but against a background drowsiness in two patients and fairly frequent 'over sleep' symptoms.

4. Family history.

In one patient a history that father (now deceased) had suffered from sleep attacks was elicited.

5. Associated symptoms.

Obesity:	Obesity was moderately marked in the two male patients, all three patients complained of
Appetite:	episodes of severe appetite increase although this was not always associated with a feeling of hunger, but more associated with a feeling of pleasure until nausea resulted.
Anxiety:	Anxiety symptoms were present in all subjects and the female
Depression:	patient had many severe depressive complaints.
vHeadache:	Headache was a chronic symptom of one of the men (Subject ⅡI) but no subject described blackouts,
Vivid dreams:	vivid dreams or insomnia.
Insomnia:	
Irritability:	Irritability was a variable symptom often associated with the episodes of hypersomnia.

6. Possibility of aetiological factors.

No significant history was obtained of any cerebral disorder. The disorder started around the time of menarche in the female patient.

7. Investigations.

a) Protein bound iodine estimations were within the normal range. Range 4.6 to 6.1 uG/100ml.

b) Skull X-rays. No abnormality found.

c) Lumbar puncture did not reveal any CSF abnormalities.

d) Haemocrit estimates were also within the normal range. Range 12.8 to 14.6 uG/100ml. blood.

e) Blood glucose estimates (at time of diurnal sleep). Mean 75mg % Range 70-76 mg %.

8. Psychiatric assessment.

In general these three young adults followed a similar pattern. Symptoms of hypersomnia with overeating, general irritability and some amnesia for events over a period of 3-4 days started at the 14-16 age period in each case at a time of family crisis or personal crisis usually in relation to school and examinations. All three patients discussed the episode as a 'depressing' time but the illness effectively took the emphasis off the practical difficulties. After this episodes of hypersomnia with or without overeating recurred at intervals often in temporal relationship to stressful events in the person's life, but clear precipitants were not available to understand every episode. The ability to sleep for lengthy periods, e.g. extended sleep, was always present and Subject I showed clear periods of compulsive eating to the point of nausea at times of personal distress without hypersomnia symptoms. No psychotic symptoms were elicited and in the hypersomnia period the subject was usually described to be irritable, drowsy and clumsy, possibly confused but not grossly disorientated. No disinhibitory symptoms were found.

Pickwickian Subjects n = 2.

M1, aged 57.

Symptoms: Drowsiness
Sleep attacks + some sudden, other gradual onset. Variable. Restless sleep. Marked snoring. (Patient has always refused to sleep away from home as his snores are disturbing). Sleep disturbance present over 20 years.

History: Involved in a car crash - March 1968. No definite history of head injury or loss of consciousness, although he received a blow on the front of the head. Off work for several months. Admitted to local hospital in September 1968 as his weight had increased to over 15 stone and he complained of dyspnoea. Skull X-ray, lumbar puncture and EEG investigations were all within normal limits. Peripheral blood values were also normal. I131 uptake measurements were also within the low normal range and a trial of thyroid extract did not help his complaint of drowsiness. Strict 1000 calorie diet was effective in reducing his weight. He returned to work but in November 1968 complained of 'attacks' involving shaking of limb, leading to possible loss of consciousness which was transitory. These 'attakcs' sometimes occurred hourly but were controlled when he was in 'fresh air'. Previous history was otherwise uneventful.

On examination: Moderate obesity. Weight 13 stone 12 pounds. Height 5 foot 9 inches. No cyanosis or finger clubbing. C.V.S. BP 105/65. Pulse regular 75/min. No peripheraloedema. Respiratory system - no abnormalities noted. Alimentary system - Normal. C.N.S. No abnormalities found.

Routine investigations: Blood. Haemoglobin 14.5 Gm/100ml. 99%. P.C.V. 48%. MCHC 30%. Reticulocyte count 4.5%. E.S.R. 13 min first hour. Platelet count 180,000/cu. mm. W.B.C. 9,300/cu. mm. Differential count within normal limits. Blood urea 28mg/100ml. Serum sodium 140 m.eg/litre. Serum potassium 4.7 m.eg/litre. Serum chloride 106.m. eg/litre Bicarbonate 27 m. eg/litre. P.B.I. 6.4 ug/100ml E.C.G. Apart from occasional supra ventricular ectopic beats the record is within normal limits.

X-ray. Skull. The pituitary fossa is within normal limits. No lesion seen in crainal vault.

Chest. No active lung or mediastinal lesion seen.

M.2. (aged 32).

Symptoms. Variable drowsiness.
Sleep attacks- some gradual in boring situations such as travelling by train or watching television. Other precipitant while active - driving his car or talking after a meal with customers when he feels motivated to be alert and active.

No cataplexy, hypnogogic phenomena or sleep paralysis.

Overnight sleep is marked by snoring - a complaint from relatives and friends.

Present - snoring nocturnal respiration can be traced back to early adult life. Then only a source of embarrassment. About 1960 (aged 22) he stopped smoking and took less exercise over a period and his weight increased to 17 stone. Dirunal somnolent episodes were troublesome after this time. On various anorectic agents he has lost several stone of weight with variable improvement. Current weight 14 stone 6 lbs.

Investigations. X-ray of skull, cervical spine and chest normal. Routine encephalograph was within normal limits. Peripheral blood counts were all within normal range.

(E.S.R. 3 min/1st hour. Haemoglobin 14.9 G/100ml., W.B.C, 8,100 cells/cumm. Platelet count normal.)

Serum electrolytes including bicarbonate were normal.

Blood urea 24mg/100ml.

Protein bound iodine 4.8 µg/100ml.

Electrocardiogram. No abnormality.

RESULTS

Part 2:

Polygraphic data

A. The patient group as a whole. n = 54.

I. Routine clinical encephalography.

A routine EEG examination under the normal clinical conditions was carried out on the patient group, usually at the point of initial referral (average duration 20 minutes).

i. Idiopathic narcoleptic group. n = 30.

	Number of Patients	
Record entirely within noral mimits for age	24	(80%)
Abnormalities		
Persistent low voltage fast activity	2	(6.6%)
Irregular slow waves at vertex and poles of cerebrium	3	(10%)
Persistent diffuse low voltage slow activity	1	(3.3%)
Evidence of drowsiness (fluctuant alpha activity and periods of low voltage flat record with occasional slow waves).	26	(86.6%)
Stage II sleep (sleep spindles at 14 cps)	6	(20%)

ii. Symptomatic narcoleptic group. n = 6.

Record normal within limits for age	1	(F1)	
Abnormalities			
Persistent low voltage fast activity	2	(M2)	(M3)
Irregular and diffuse slow activity	2	(M1)	(F2)
Severe localized slow activity	1	(M4)	

Evidence of drowsiness	5
Stage II sleep	2

iii. Patients with idiopathic hypersomnia n = 13.

Record within normal limits for age	9
Abnormalities	
Evidence of frontal fast drug induced activity	3
Low voltage persistent flat record	1
Drowsiness	5
Stage II sleep	0

iv. Pickwikkian syndrome subjects n = 2.

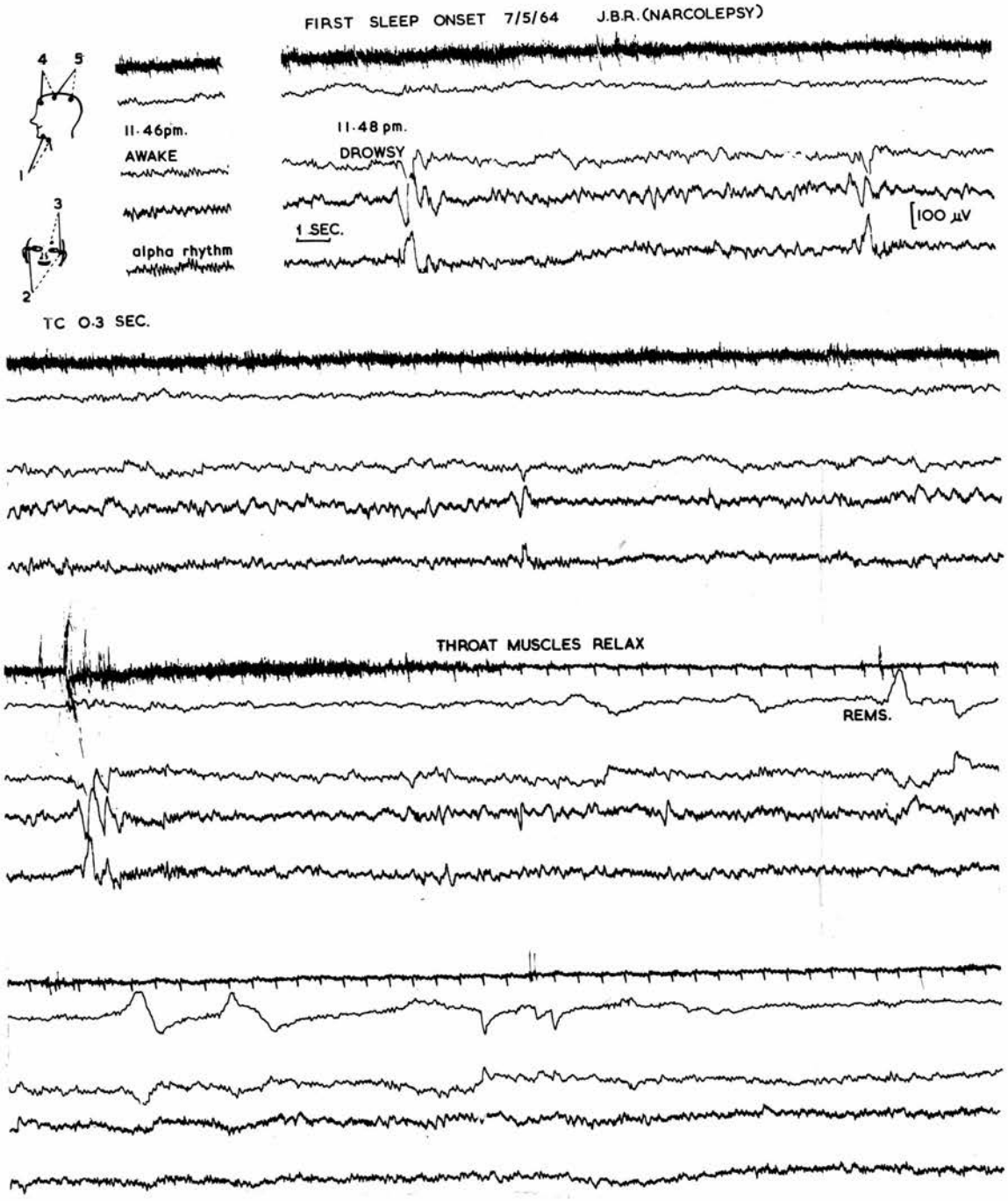
Record within normal limits	1
Abnormalities	
Very low voltage record	1
Drowsiness	2
Stage II sleep	0

v. Kleine Levin syndrome subjects n = 3.

Record within normal limits for age	3
Abnormalities	
Drowsiness	1
Stage II sleep	0

II. First night in the laboratory n = 54.

i.	Sleep onset REM sleep i.e. REM sleep developing within a few minutes of start of recording.	17	(32.1%)
ii.	Respiratory abnormalities sufficient to disturb the continuity of sleep	2	(3.6%)
iii.	Abnormal short latency to first REM period (less than 45 mins)	7	(13.2%)
iv.	No significant abnormality	27	(51.3%)



IDIOPATHIC NARCOLEPSY. SOREM PERIOD. THE VERY FIRST RECORD OBTAINED BY DR. OSWALD AND MYSELF IN 1964 WHICH STARTED THIS STUDY

III. Sleep studies related to clinical diagnosis. (Full data is presented in Appendix II).

(a) The idiopathic narcoleptic group. n = 30.

i) Sleep onset REM sleep periods.

	Subjects	
Present on first night	17	(56.6%)
Second laboratory night	20	(66.6%)
Third laboratory night	27	(90%)
Fourth laboratory night	29	(96.6%)
Sixth laboratory night	30	(100%)

ii) Regularity of REM sleep onset.

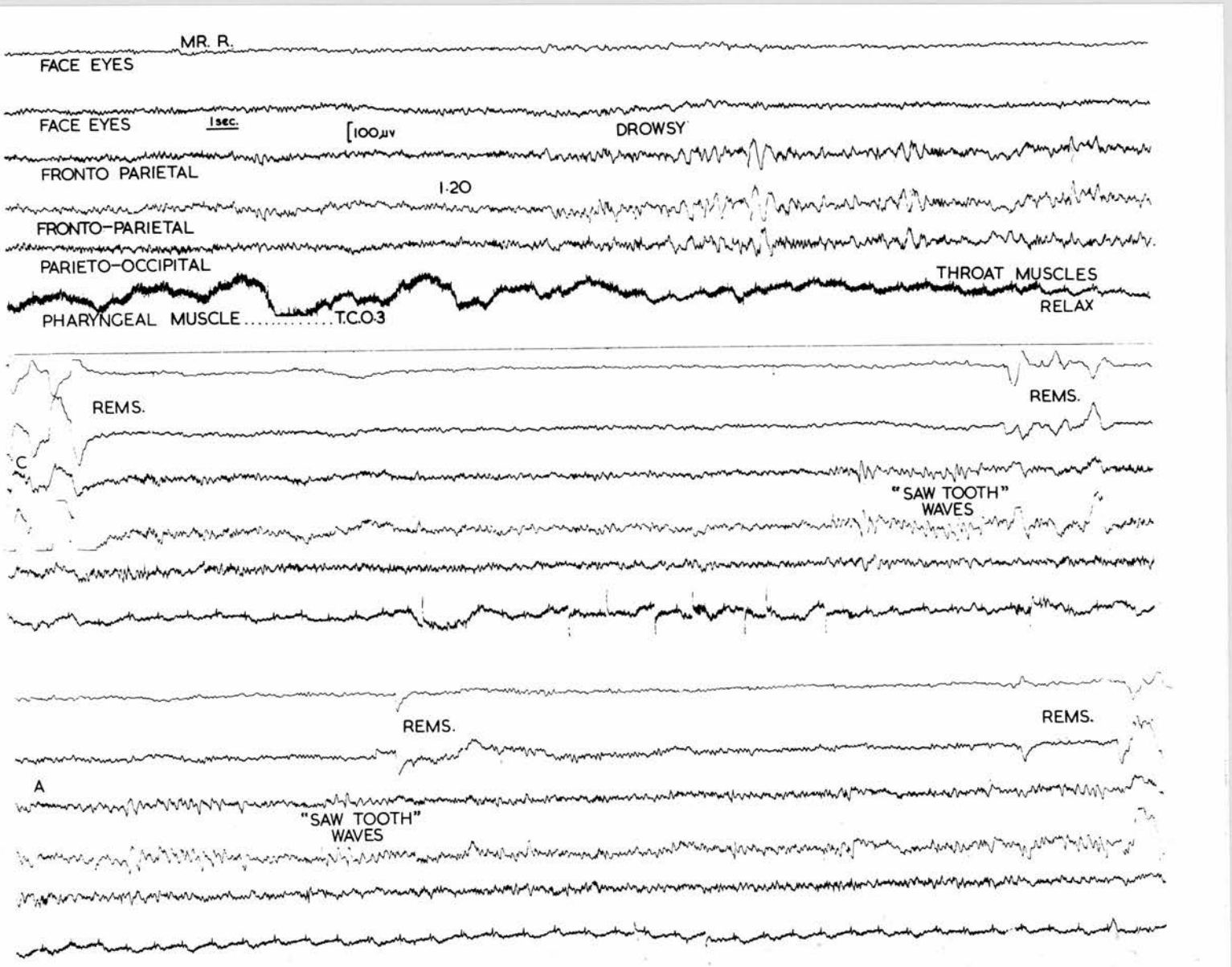
Although this abnormality frequently failed to appear in the initial records, further records after it was recognised usually confirmed the presente of the abnormalities. However on some occasions sleep onset REM periods (SOREMP) failed to emerge. Discussion with the patients revealed several reasons for this variability:-

1) A period of sleep within 2 or more hours of the start of the recording (e.g. sleeping on a bus on the way to the laboratory) frequently aborted the SOREMP or resulted in a very fragmented SOREMP.

2) Factors which raised the 'novelty' of the recording situation also severely restricted the SOREMP period e.g. moving from the usual laboratory to another, introducing strangers as 'observers' into the recording situation or any unexpected disturbance in the laboratory itself.

3) Severe anxiety due to outside factors in the patients world can severely affect the sleep in the laboratory.

4) In an attempt to prevent sleep prior to the recording some patients spent part or the whole of the day prior to the recording night in the adjacent ward. It then became clear that there were occasions when the staff noted short lived sleep periods which were not reported by the patient and these also limited or obliterated the SOREMP period at the start of the night.



IDIOPATHIC NARCOLEPSY. SLEEP ONSET REM PERIOD. AN 'ATTACK' OF NARCOLEPSY AFTER LUNCH

iii) SOREMP developed either at the start of the recording (or more frequently after a few minutes of Stage I sleep in which rolling eye movements occurred and the encephalogram was composed of some slow waves and other fast frequencies. Rarely was this 'descending' Stage I period greater than 6 minutes duration.

Mean = 3.2190. Standard deviation = 3.4334 min.

On several isolated occasions in this series a short period of Stage II sleep (less than 2 mins) with definite sleep spindles preceded the REM sleep period.

iv) Duration of the SOREMP sleep period.

1) In subjects not on any therapy.

Mean SOREMP = 12.6888 min.

SD 6.3918 min.

2) In patients taking sympathetico mimetic drugs.

Mean SOREMP = 10.9318 min.

SD 7.3021 min.

The difference between these SOREMP is not significant (d = 87. t = 1.2086. p >0.3).

v) The physiological features of the SOREMP were identical with REM sleep periods seen later in the night in each subject. During the remainder of the night sleep in the narcoleptic subjects REM sleep periods alternated regularly with periods of slow wave sleep.

(b) <u>Narcoleptic subjects and control group</u>.

For further comparison purposes, the first 15 subjects in the idiopathic narcoleptic group (8 female, 7 male, age range 22-55 years, mean 32.5 years) were matched for age and sex with a control group. Subjects in the control group slept for two nights in the laboratory at an interval of more than one week, and also attended the laboratory on two occasions at 12 midday and were recorded in the preprandial period under the same conditions as the narcoleptic patients.

1) No control subject showed SOREMP sleep.

2) Sleep onset (i.e. the first evidence of sleep spindle activity) occurred with a latency of 21.8 minutes in control subjects. (Mean = 21.8333 min. SD = 16.2949 min.). In narcoleptic subjects, latency to first spindles.

Mean = 28.1190 min.

SD = 24.6296 min.

This is not significant (df 122. t = 1.3227. p = 0.1)

3) Percentage of REM sleep in whole night.

Narcoleptic Group (n = 15)

Mean = 24.4489 % of total sleep

SD 3.6957 %

Control Group (n = 15)

Mean = 21.3758 %

SD = 4.0101 %

This is significant (df = 75. 5 = 3.8203 $p < 0.001$).

4) Percentage of Stages III + IV sleep in whole night.

Narcoleptic Group Mean 21.8069 % of total sleep
SD 3.5181 %

Control Group Mean 18.3900 %
SD 5.8705 %

This difference is significant
(df = 71. t = 2.1051. $p < 0.025$).

5) Shifts to Stage I or Awake, per hour during total night.

Narcoleptic group. Mean 3.7558 shifts/hour
SD 1.2249

Control group. Mean 3.9783 shifts/hour
SD 1.0933

This difference is not significant
(df = 67. 5 = 0.7832 $p < 0.50$).

6. Removal of the SOREM period from the total REM sleep for the narcoleptic group.

Narcoleptic group Mean 22.9931 % total sleep
SD 4.0367 %

Control group Mean 21.3758 % total sleep
SD 4.0101 %

The difference between these groups is not significant (df 71. t = 1.6794. p = 0.10).

7. Distribution of REM sleep over the remainder of the night.

No significant differences could be found between the narcoleptic and control groups.

(c) <u>The effects of drugs on the sleep of narcoleptic</u> subjects n = 30.

i. <u>The effect of chronic use of sympathetico-mimetic drugs on REM sleep</u>.

Percentage REM sleep in 'No drugs' group. (n = 14).
Mean 24.9500 % of total sleep
SD 3.5211 %

Percentage REM sleep in patients taking sympathetico-mimetic drugs. (Amphetamine n = 14, methylphenidate n = 2).

Mean 25.4446 %
SD 4.0167

These differences are not significant (df = 90. t = 0.6042. $p < 0.3$).

ii. Effect of sympathetico-mimetic drugs on SOREM sleep (n = 30).

SOREMP in 'no drugs' group. Mean = 12.6888 mins.
(n = 14) SD 6.3918 mins.

SOREMP in 'drug' group
(Amphetamine n = 14) Mean = 10.9318
(Methylphenidate n = 2) SD 7.3021.

Difference is not significant.

iii. Effect of stopping drug (amphetamine) on initial SOREMP. This was possible in five narcoleptic patients (n = 5).

SOREMP, on drugs	Mean	14.9333 mins.
	SD	5.0774
SOREMP in first 10 days of drugs	Mean	18.1975 mins.
	SD	9.8942
SOREMP in period of over 14 days off all drugs	Mean	13.9000 mins.
	SD	4.9542

The difference between SOREMP on drugs and SOREMP in the first 2 weeks of withdrawal significant only at the $p = 0.10$ level. (df 23. $t = 1.0847$).

iv. Effect of a loading dose of 5G. laevo tryptophan on SOREMP (n = 30).

		Tryptophan 5G.	Nil
a) on 'no drugs' group	Mean	26.2200 mins	12.6888 mins.
	SD	12.2895	6.3918
b) on 'drugs' group (amphetamine and methylphenidate)	Mean	18.4722 mins	10.9318 mins.
	SD	6.4519	7.3021

The difference between SOREMP in the 'no drugs' group with and without 5G tryptophan is significant (df 93. $t = 6.6215$. $p < 0.0005$).

The difference between SOREMP in the 'drugs' group with and without 5G tryptophan is also significant (df 78. $t = 4.8392$. $p < 0.0005$).

The effect of an oral dose of laevo tryptophan on the group receiving no treatment and the group receiving amphetamine/methylphenidate, is also significant (df = 84. $t = 3.4519$. $p < 0.0005$).

v. The effect of removal of amphetamine on the tryptophan sensitibity of the narcoleptic patient.

Tryptophan 5G.

SOREMP, on drug — Mean 18.4722 mins.
SD 6.4509

SOREMP, after 2 weeks off drug — Mean 26.2200 mins.
SD 12.2895

This difference is significant
(df 84. t = 3.4519. p<0.0005).

vi. Effect of Methysergide (Deseril) on SOREMP and on tryptophan load sensitivity (n = 8).

SOREMP, no drugs — Mean 14.9565 mins.
SD 7.8594

Methysergide (6mg) — Mean 13.4615 mins.
SD 7.1135

SOREMP 5.G. Tryptophan load — Mean 28.0176 mins.
SD 3.2787

Methysergide (6mg) + 5G. Tryptophan load. — Mean 26.8535 mins.
SD 2.9957

The effect of Methysergide on tryptophan sensitivity is not significant.
(df = 41.0 t = 1.2001. p <0.10).

The effect of Methysergide on SOREM period is not significant (df = 34 t = 0.5665 p<0.3).

vii. Effect of Imipramine on SOREMP (n = 3).

SOREMP 'no drugs' — Mean 13.3333 mins.
SD 6.1644

SOREM. 'imipramine' 50mg daily.
Mean 5.0000 mins
SD 5.1345

The difference is significant.
(df = 19. t = 3.3799. p< 0.005).

viii. Effect of methylphenidate (Ritalin) in SOREMP (n = 4).

SOREMP, on no drugs — Mean 18.8750 mins.
SD 5.9166

On Ritalin 10mg BID — Mean 3.9166 mins.
SD 4.8328

This differance is significant (df = 18. t = 6.1703 $p < 0.001$).

ix. Effect of methylphenidate on tryptophan sensitivity. SOREM sleep. Methylphenidate 20mg.

Mean 3.9166 mins.
SD 4.8328

SOREM sleep Ritalin 20mg. + 5G 1. tryptophan — Mean 12.2857 mins.
SD 2.1380

The difference is significant $p < 0.001$ (df = 17. t = 4.3028).

(d) Diurnal sleep in narcoleptic subjects and in control group. Overall subjects n = 30.

(a) Slept in laboratory on 45 occasions - 38 at noon; 4 at 1700 hours and 3 during the evening.

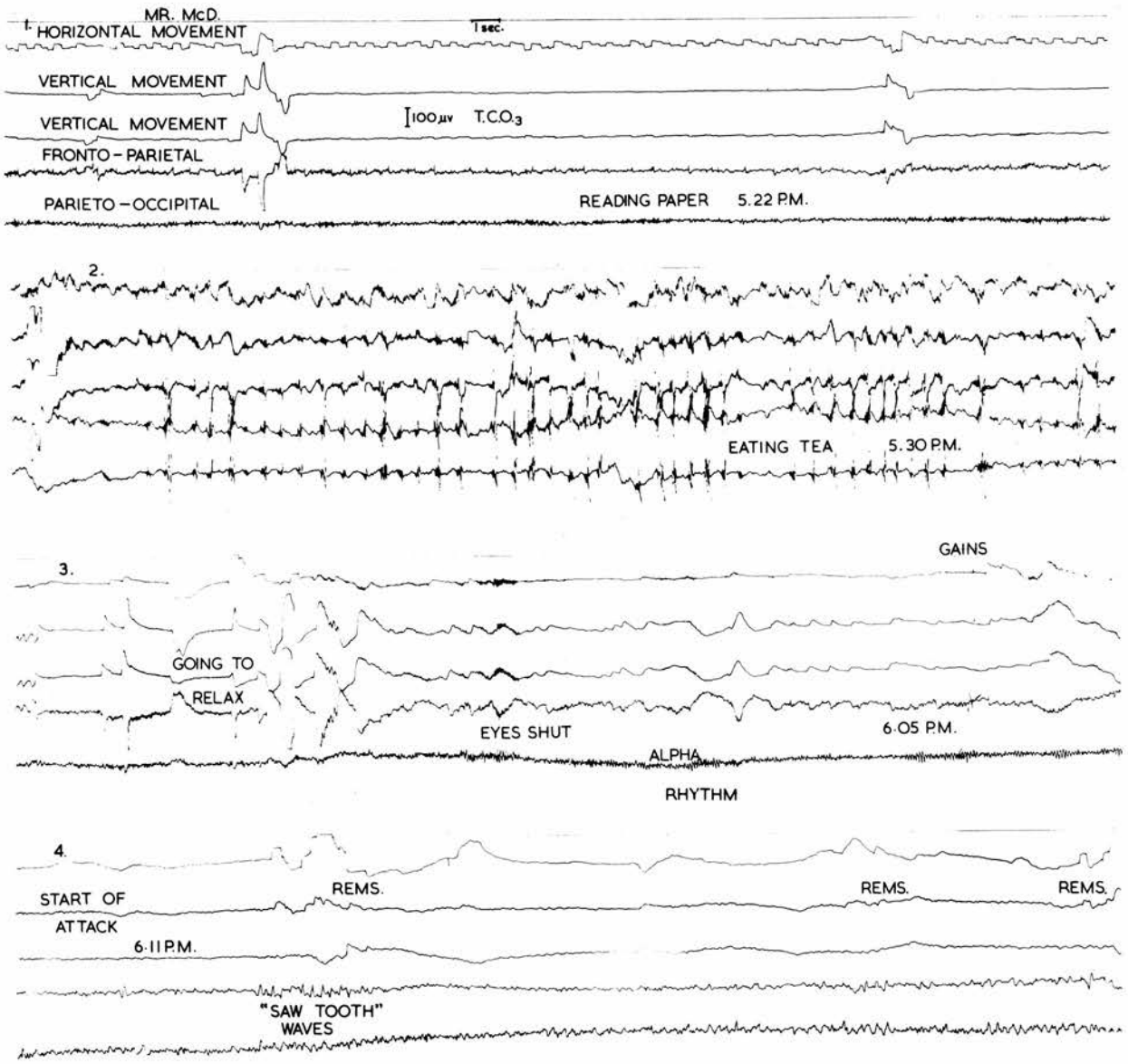
(b) SOREM periods occurred on 39 occasions (86.6%)

Duration of SOREMP — Mean 9.8205 mins.
SD 6.6287

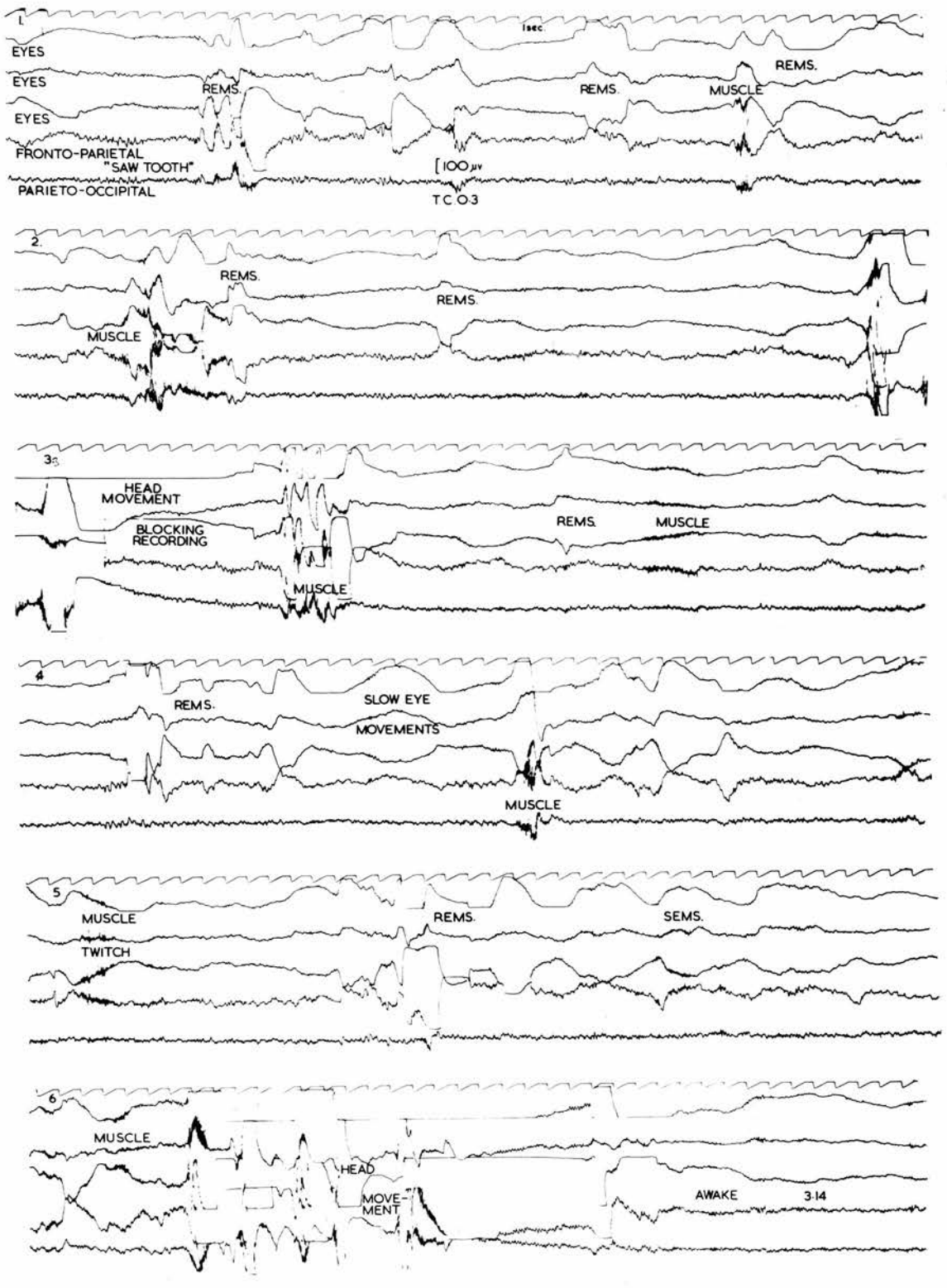
(c) Sleep (either REM or slow wave sleep) was recorded in 100% of narcoleptics and 66% of the control group (n = 15) who slept in the laboratory on two occasions during the day. No subject on the control group developed any REM sleep during the period of recording.

(d) In the narcoleptic group SOREMP developed immediately or after a few moments of descendant Stage I sleep.

Mean = 3.4864 mins
SD = 1.9382



RECORDING SLEEP ATTACK. STRIPS OF RECORD WHILE READING, EATING A MEAL AND RELAXING. SOREMP THEN DEVELOPED. GAINS WERE INCREASED TO FULL WHEN SUBJECT WAS DROWSY



A SPONTANEOUS ATTACK OF NARCOLEPSY. CONTINUOUS RECORD LASTS LESS THAN 2 MINUTES. REM SLEEP IS ASSOCIATED WITH BURSTS OF MOVEMENTS AND MUSCLE ARTIFACT

(e) The relationship of SOREM periods and the hypersomnia group in general. Comparison of SOREM periods with symptoms in the various classes of hypersomnia shows that with one exception SOREM periods are found in patients suffering from idiopathic narcolepsy. The single exception was one patient with a post encephalitic illness. Further, in the patients with idiopathic narcolepsy SOREM periods correlate with the symptom of cataplexy, complete or partial. There were three patients in the group in whom a definite history of cataplexy was absent. One patient however complained of sleep paralysis and in both the remaining cases, discussion with the patient revealed that mild cataplexy symptoms had occurred infrequently in the past but their significance was not apparent to the patient.

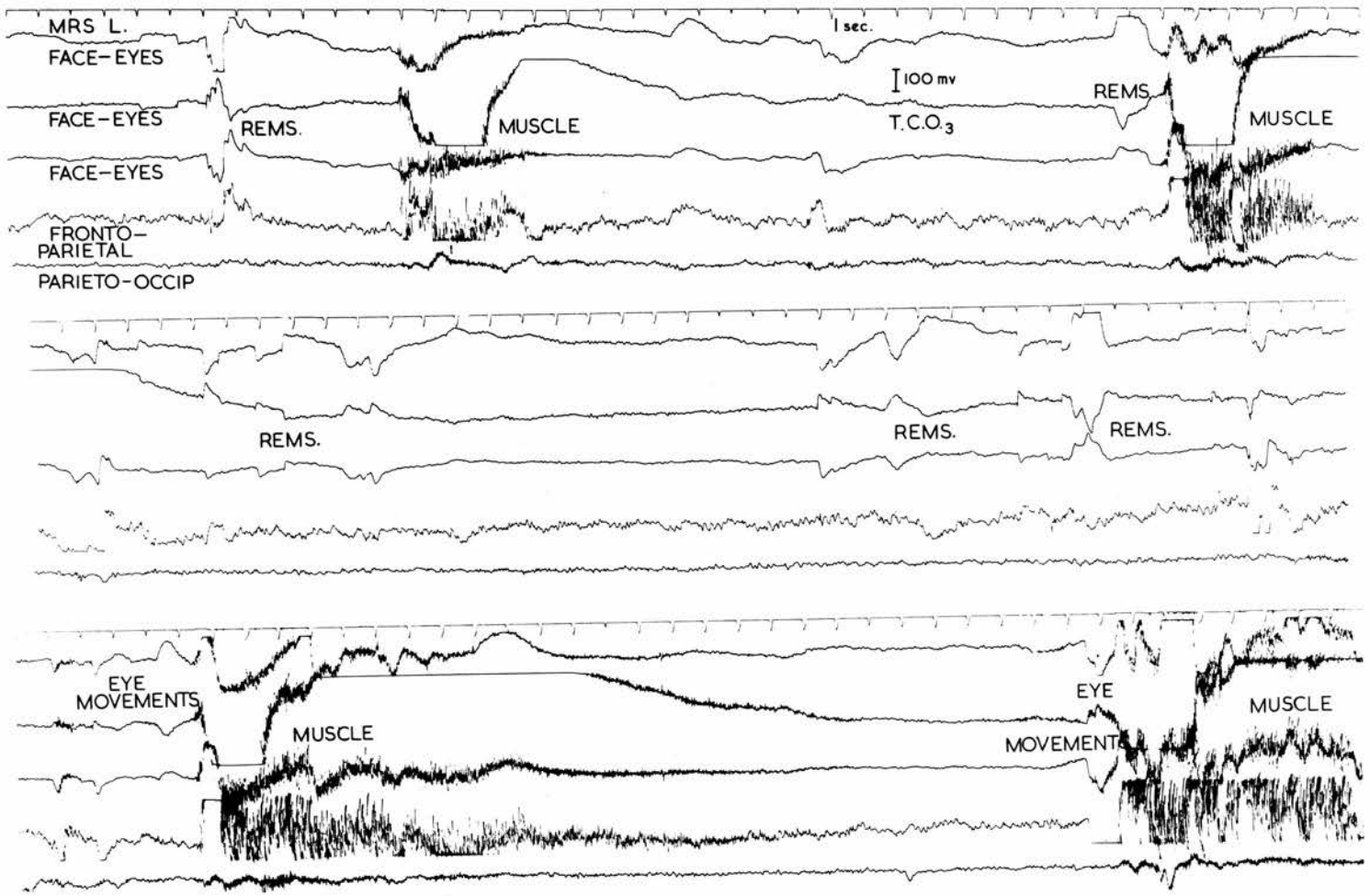
(f) Narcolepsy symptoms in relation to REM sleep.

On a number of occasions, particularly in the diurnal recording sessions, idiopathic narcoleptic patients woke spontaneously either at the end of a SOREM period, or after a few minutes of Stage II sleep following a SOREM period. By design there was a maximum length imposed on the preprandial recording by the arrival of a nurse to serve lunch to the patient. The original purpose of this arrangement was that a natural 'lull' between 12.30 and 1300 hours would occur in which the patient could read seated in a chair or at a table while waiting for lunch. It was not specifically put to the patient that a sleep attack was to be investigated. On waking patients were asked immediately to report what had been happening and in this way reports of narcoleptic symptoms were collected.

Phenomena in diurnal sleep attacks (n = 30). Recordings = 45. SOREM occurred in 39 recordings.

1. <u>The denial of sleep</u>

On 8 occasions (17.7%) always after SOREM period lasting less than 10 minutes, subjects denied sleep. Although the stock question was 'what has been happening? The standard denial reply was 'I wasn't asleep, just thinking', almost an automatic denial defence. Thinking ranged over a number of topics related to the subject, the experiment, lunch and the arrival of the nurse. In 3 instances, denial of sleep was associated with the/



SLEEP PARALYSIS. REM SLEEP CONTINUOUS WITH BURSTS OF MUSCLE ACTIVITY AND SOME MOVEMENT AGAINST BACKGROUND OF LOW MUSCLE TONE

/the claim that the experimenter or a colleague had entered the recording room to adjust an electrode or some other equipment. While the process appeared to be a denial defence it was also apparent that patients were frequently unaware of their sleep attack.

2) Sleep paralysis.

On 6 occasion (13.3%) subjects woke spontaneously from SOREM period and reported sleep paralysis in graphic style. For example, F6 gave the following account:-

> "I've been awake ages. Couldn't move. I've tried to call you again and again. There was this horrible thing - black like a big spider - long wriggling tentacles like an octopus over there on that chair. Then they were fronds of seaweed. Wet and slimy. I couldn't move away from them".

The polygraphic record of the whole period of thirteen minutes contained initially 2 mins of descending Stage I sleep and eleven minutes of active REM sleep marked by bursts of muscle and movement artifact between the eye movement bursts. (FIG.). Frequently after a movement transitory alpha rhythm occurred, quickly replaced by REM sleep and there was no clear period of arousal. Yet it is typical of sleep paralysis that the individual claims to be wide awake despite hypnogogic difficulties. However accounts of sleep paralysis have only occurred in this study when the subject awoke out of a REM sleep period marked by transitory but often intense bursts of muscle activity, muscle tone otherwise remaining low, i.e. after a great increase in phasic activity but not in tonic activity.

3) Hypnogogic hallucinations.

The most frequent hypnogogic hallucination particularly in the group who denied having slept was that the experimenter or another person had entered the room and touched or adjusted the patient's electrodes. Accounts of someone bending over the patient or of a figure standing in the doorway watching the subject were also frequent.

Such phenomena occurred exclusively in association with SOREM periods and slow sleep periods were never eventful, although Stage I sleep was found in all cases. This makes the division of hypnogogic hallucinations and dreams extremely difficult.

4) Dreaming./

4) Dreaming.

Dreams were frequently reported on 30 occasions (84.3%) spontaneously or by a process of deduction by patients. They were exclusively found after SOREMP, never after slow sleep periods. In some ways they were different from dream reports obtained during nocturnal sleep.

Examples:

Subject M3. "I was sitting here waiting for the nurse to bring in lunch. It was hot and pleasant, sun shining through the window and I felt relaxed and happy. Sister came in with a tray. She put it down on a table at the door, sat down and started to eat my lunch. I was amazed, felt angry, tried to shout.....couldn't..... couldn't move. I tried and tried and then woke up".

This dream in fact starts in reality - he was sitting waiting for lunch on a summer's afternoon. The expected - Sister with a lunch tray appears, but the remainder is fantasy - there was no table or chair at the door and lunch had not arrived when he woke spontaneously. Subject realized the fantasy incorporated in the dream as such and told the story with a laugh.

Subject F6. "It was evening. You came in and took off my electrodes and said I was free until time for bed. I looked at my watch - it was nearly 6.00 p.m. I remembered that my cousin from Canada was going to 'phone about six so I walked down the corridor and out into the car park. I went to the main door of the hospital to be near the main telephone exchange. There was a clock above the desk - it said 5.35 - I thought my watch was wrong, so I just sat down on a settee in the hall to wait".

This dream is extremely reality based. It was in fact 6.00 p.m. and this late afternoon sleep was due to finish about that time. This patient had already told me of the anticipated call as I set up the electrodes and the account of her walk is quite accurate. However there is no clock in the hall she described, no settee or chair either. The whole dream is a fulfillment of anticipated action and so based on reality that for some hours this patient wasn't sure whether it was a dream or reality.

Subject F5. "I was on a ship. It was a lovely warm day and my husband and some other people were/

/were sunbathing on deck. Suddenly there was a shout and alarm bells rang. The ship was sinking. It was awful, nobody knew what to do and they ran around. They tried to let down the lifeboat but the pulleys were jammed. My husband got a life jacket for me and we jumped into the water. Lots of people were swimming and I got onto a sort of raft. It was quiet again".

This is an excellant example of dream incorporation. It had been a hot day, after this subject had been in SOREM for approximately 2 mins., three fire engines pulled into the hospital grounds and drove down to the laboratory with their alarm bells ringing. Firemen got out and some went behind the laboratory while others fixed a hose to a hydrant immediately under the laboratory window. Two fire engines then drove on leaving the third to act as a pump. Throughout this noisy period the patient continued to show REM sleep and made occasional movements. All the noises of the incident occur clearly in the dream which contains the fluctuating anxiety level appropriately to the incident. To the patient it was a vivid rather nightmarish dream.

Subject M1. This patient suffered from a paranoid illness. "I was sitting on the chair wondering whether it was time for lunch. I had forgotten my watch. You came in and did something behind my head - I thought there was a machine there. I tried to turn to see what you were doing but my head was heavy and fell forward. Sister came in with lunch and you spoke together. I knew it was about me. She went out and I saw you put a pill into the teapot. I tried to shout but couldn't."

This patient reported this experience as a dream. It contains much reality, but goes on to events which, up to a point were expectable - I might have come back into the room and Sister was due to bring in lunch. But the fantasy increases in a distinct paranoid way. Several days later he openly accused another doctor of poisoning his food.

These examples illustrate some of the principle features of the dream of the SOREM period.

1. They begin frequently in reality./

2. As the dream develops it contains reality concepts in terms of what is expected or could happen.

3. From this more fantasy material becomes mixed with reality based material and the dream progresses in a wish fulfillment fantasy.

4. Vivid dreams and nightmare qualities of powerlessness and threatening fantasy occur frequently.

5. Incorporation of environmental stimuli occur and add further reality to the dream which frequently leaves the patient in some doubt whether the experience was real after all.

5. Cataplexy.

Despite many attempts to induce cataplexy in subjects, no definite incident of total cataplexy was in fact recorded. Sudden startless, or arousing emotion - anger or laughter did frequently make the subject complain of feeling weak but despite recording in a standing position, no total loss of tone occurred.

However short periods of loss of tone could be recorded in narcoleptic subjects both in standing recordings and when seated. These were frequently limited to head and neck and reported by patients as 'my face was weak and distorted', or 'my head felt very heavy and fell forward'.

Tone returned abruptly to the involved muscles and on some occasions a full picture of SOREM period developed rapidly.

6. General drowsiness.

Sleep was recorded on 100% of the diurnal recording opportunities with the idiopathic narcoleptic group. SOREM periods developed in 86.6% of occasions but in the remaining instances slow wave sleep developed frequently with a very short latency.

Diurnal sleep was not recorded until the subject had spent at least one night in the recording situation.

In contrast to the original clinical EEG recording where only early drowsiness was found frequently and/

/and clear evidence of slow wave sleep occurred in 20% of these patients, definited sleep occurred in 100% of the same group when they were familiar with the situation and presumably any attendant anxiety had settled.

7. Prolonged sleep.

As most patients in the narcolepsy group were working, overnight sleep was limited to about 500 minutes on most occasions. At week-ends it was possible to allow the subject to 'run on' and several subjects were able to take sleeps of 600 minutes or so. Chosing a suitable subject who reported that she could sleep for most of the day, a record of sleep starting at 23.27 hours until 10.22 hours two days later was obtained. In this time there were several periods of arousal for meals or toilet necessities but the subject returned to bed and to sleep of her own will.

A. Total period.

Start 23.27 hours 1.11.68

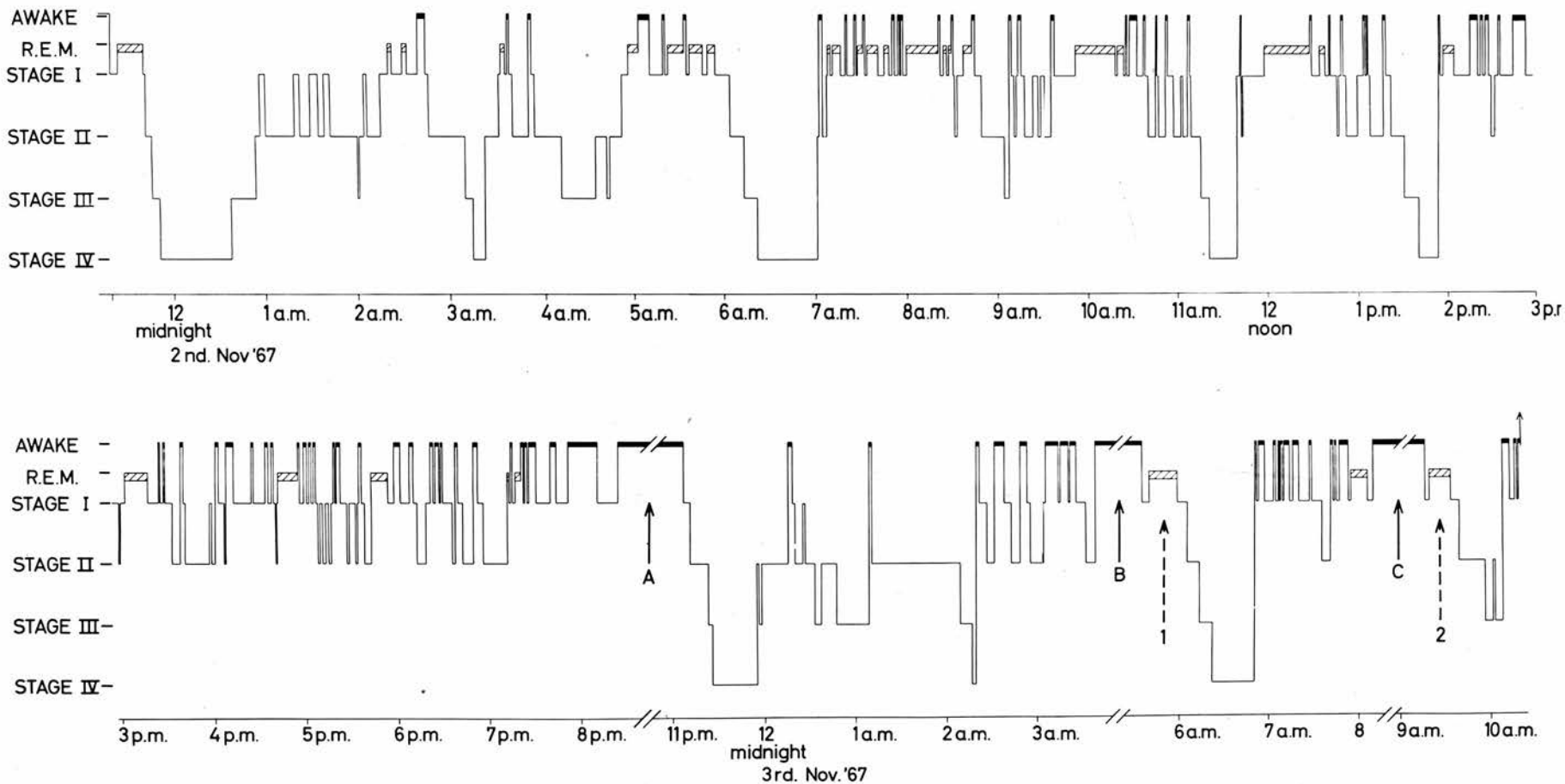
Total. Time in bed,	1770 minutes	
Total sleep time,	1338 minutes	
Awake	86 ~~minutes~~ times	
Time awake	232 minutes	(17.3%)
REM sleep	261 minutes	(19.5%)
Stage II + IV sleep	336 minutes	(25.1%)
Shifts to Stage I or Awake	3.46/hour	

B. Breakdown:

I. First sleep period 23.37 hours to 7.58 hours.

T.T.B.	511 mins.	
T.S.T.	485 mins.	
A	13 mins.	
TA	24 mins	(4.9%)
REM sleep	81 mins	(16.7%)

THE LONG SLEEP



Stage III + IV	146 mins (30.1%)
Shifts to Stage I AW/hour	2.66
Delay to sleep (d) = 0.	
Delay to next REM period	160 mins

SOREM period 16 mins developed after 5 mins descending Stage I sleep.

II. Second period (continuous with period I) 7.58 hours to 20.26 hours.

T.T.B. = 508 mins.
T.S.T. = 352 mins.
A = 53
T.A. = 156 mins (44.3%)
REM = 137 mins (38.9%)

Stage III + IV = 65 mins (18.5%)

Shifts/hour = 3.66

Awake for toilet, exercise and a meal 20.26 to 23.08 hours (A).

III. Third sleep period 23.08 hours to 3.38 hours.

T.T.B.	270	
T.S.T.	246	
A.	6	
T.A.	24 mins.	(9.8%)
REM sleep	0	(0%)
Stage III + IV	78 mins.	(31.7%)
Shifts	2.33/hour	
Awake	3.38 hours to 5.32 hours reading (B).	

Fourth sleep period 5.32 - 8.07 hours.

T.T.B.	215 mins.
T.T.S.	194 mins.
A.	11
T.A.	21 mins (10.8%).
REM sleep	29 mins. (14.9%).
Stage III + IV sleep	36 mins. (18.6%).
Shifts	5.66/hour
Awake	8.07 to 9.16 hours (talking and reading). (C).

Fifth period of sleep.

T.T.B.	66 mins.
T.S.T.	59 mins.
A.	3
T.A.	7 mins. (11.9%).
REM sleep	14 mins. (23.7%).
Stage III + IV	9 mins. (15.3%).
Shifts	3.0/hour.

Got up and said she could still sleep. After going home to change and have a meal returned to laboratory at 13.50 hours. Set up as for diurnal sleep. Delay to sleep 0. SOREM period 11 mins. developed after 2 mins descending Stage I sleep. Woke spontaneously.

Noteable in the record is that the REM sleep periods are regular and the inter REM sleep interval is approximately 90 mins. Even after such a long initial sleep, subject had SOREM periods at 5.38 hours 2.11.68 (1) and again on 9.20 (2).

8. Further data from all night sleep studies.

(a) the latency to the second REM period. When SOREM periods occurred, the latency to the next REM period was of the order of 100 minutes, Mean 78.3924 mins. SD 33.5885. However, in the absence of SOREM sleep, latency to the first REM period (D) was frequently less. Mean 59.1563 mins. SD 24.7596, and on some occasions was below the accepted minimum in the normal of 45 minutes (Oswald, 1963). This difference is significant (df 188. $t = 3.0722$ $p < 0.005$).

(b) Subsequent REM sleep periods occurred at reasonably regular intervals throughout the remaining sleep period with a mean inter REM interval of 90 minutes.

(c) Mental activity of REM sleep and slow wave sleep. In the initial group of 15 narcoleptic and matched controls, it was possible by selecting the moment of arousal in the morning to record mental activity from both REM sleep and slow wave sleep (usually Stage II or Stage III). This obviated the difficulty of disturbing the subject unduly during the night which would necessarily have distorted the other measures of sleep such as the percentage Stage REM sleep.

i. Reported mental activity in narcoleptic group which directly from REM sleep.

Awakenings	18
(a) Reports of mental activity with marked fantasy/disorientation or clearly described by subjects as dreaming	14 (77.7%).
(b) No mental activity admitted	3 (16.6%).
(c) Reports of 'thinking'	1 (5.5%).

ii. Reports of mental activity in controls awaking from REM sleep.

Instances	15
(a) Reports of mental activity showing marked fantasy/ disorientation or labelled by subject as a 'Dream'.	11 (73.3%).

(b) Mental activity denied 4 (26.6%).

iii. Reported mental activity when wakened from SW sleep (Stage II or III). Narcoleptic group n = 15.

Instances 12

(a) Mental activity showing marked fantasy/disorientation or labelled as a dream. 2 (16.6%).

(b) Mental activity denied 8 (66.6%).

(c) Reports of 'thinking' 2 (16.6%).

iv. Reported mental activity when awakened from slow wave sleep (Stage II or III). Control group = 15.

Instances 10

(a) Mental activity showing fantasy/dissorentation or labelled as (dream'. 1 (10%).

(b) Mental activity denied 8 (80%).

(c) Reports of 'thinking' 1 (10%).

No significant differences between the mental activity of REM sleep or slow wave sleep in narcoleptic patients and in control subjects was apparent.

SYMPTOMATIC Narcoleptic group n = 6.

In several subjects in this group it was only possible to record sleep on a limited number of occasions as these subjects were not prepared to co-operate over a lengthy period of time even though I personally collected them from their homes and returned them in the morning.

a) SOREMP.

In only one subject were signs of SOREM sleep seen. Subject F1 usually after a short period descending Stage I sleep showed a fall in submental tone often to zero, accompanied by runs of 6 cps activity in the frontal regions and some small isolated eye movements. The episodes were transitory and complete within 1 minute. While the physiological changes were in keeping with REM sleep seen later in the night, the transitory nature of the sleep onset changes was a marked feature of all recordings.

b) Delay to sleep.

Apart from subject F1 who slept immediately the latency of sleep (i.e. first sleep spindles) was frequently over 20 minutes (Mean 31.9474 mins. SD 27.1221. Range 4-96 minutes). Subject M2 showed excessively prolonged sleep latencies of 51-90 minutes.

c) Delay to First REM sleep period (D).

Latency of the first REM sleep period was usually of the order of 100 minutes (Range 56-280 mins. Mean 143.3478 min. SD 127.5021 mins.

d) Amount of sleep.

In relation to the amount of time available, these patients slept to a variable extent. Some subjects (e.g. F1, M4, M3) normally slept approximately 90% of the time available, while others (e.g. M2, F2) slept as little as 50% of the time available.

e) Awakenings and shifts.

On the whole, the group slept poorly, wakening about/

/about 5 or 6 times a night for short periods. Subject M2 woke very frequently (4-26 times) for up to 138 minutes. Shifts to arousal or Stage I sleep occurred 3/4 times an hour in the group (Mean 3.9969 SD 1.4802).

f) The amount of slow wave sleep - Percentage III + IV. Range 6.1 - 42.6%. Mean 21.3045% SD 13.1146% The variability was aged linked i.e. Subject M4 aged 16 years spent 36-42% of the night in Stage III and IV slow wave sleep, while subject M4 (aged 60) spent less than 9% of the night in these sleep stages.

g) <u>The amount of REM sleep.</u>

Range	16.0 - 28.7% of total sleep
Mean	22.5651%
SD	3.9148%

h) The effect of a loading dose (5G) of laevo tryptophan. A loading dose of l-tryptophan was given on occasions to each subject. No significant effects were found.

i) <u>Sleep in the day.</u>

With the exception of subject M4 who was involved in an extensive rehabilitation and re-education programme at the time of the study, and not available in the day and not prepared to attend in the evening, all subjects slept in the laboratory during the day. Under conditions set up for the idiopathic narcolepsy group at 12 noon or 17.30 hours, these patients were also drowsy.

Recordings	17.	
At 12 noon	11.	
17.30 hours	3.	
19.30 hours	3.	
SOREM periods	2.	(Subject F1 only)
Persistent drowsiness	8.	
Slow wave sleep Stage II alone	6.	
Stage II + III	1.	

One subject showed a REM sleep period of 9 minutes with a latency of 60 minutes from the start of sleep.

j) Mental activity during REM sleep and slow wave sleep.

Wakenings from REM sleep	7	
(a) Mental activity involving fantasy/ disorientation	4	(57.1%)
(b) mental activity denied	2	(28.5%)
(c) mental activity described as 'thinking'	1	(14.3%)
Wakenings from slow wave sleep (Stage I or II) =	6	
(a) Mental activity involving fantasy disorientation	1	(16.6%)
(b) mental activity denied	4	(66.4%)
(c) mental activity described as thinking	1	(16.6%)

Idiopathic Hypersomnia n = 13.

a) SOREM periods.

NO SOREM periods were recorded.

b) Delay to sleep (d)

Range	0. - 36 mins
Mean	16.7037 mins.
SD	13.7259 mins.

c) Delay to REM sleep (D).

Range 38 - 210 mins.
Mean 88.9804 mins.
SD 35.3392 mins.

d) The amount of sleep.

In general this group slept 80-90 % of the time available for sleep. The exception, Subject M2 frequently slept from 70-80%cof the time available.

e) Wake periods.

In general the continuity of sleep was good. Number of arousal periods usually less than 6 per night and time awake frequently less than 10 mins. Number of arousals/night, Mean 2.4 Time awake/night, Mean 13.46 mins.

f) Shifts to Awake or Stage I per hour.

Range	1.0 - 5.83 Shifts/hour
Mean	3.1535
SD	1.5130

g) Amount of slow wave sleep. Stages III + IV.

Range	11.4 - 36.8%
Mean	21.6975 % of total sleep.
SD	6.2697%

h) Amount of REM sleep.

Range 12.8 - 34.4%

Mean 23.9585 % of total sleep

SD 3.7158 %

It was noted that the extremes of the range of REM sleep and slow wave sleep occurred in Subject F4 (aged 6 years), F5, F6 and M7.

i) Extended sleep (n = 8).

It was possible in eight subjects in this group to extend the time available for sleep from the normal 500 minutes or so to 720 minutes and on one occasion (F1) to 844 minutes. Under these circumstances these patients were able to extend their sleep to occupy only 88.33% of the time (against afmean of 95.4% SD under normal conditions). The number of arousals and time awake increased. Mean number of arousals 13.33. Mean time awake 71 mins. The amount of Stage III+ IV S.W.S. fell to a mean of 18.0000% of total sleep, SD 5.3198 %. The amount of REM sleep rose slightly. Mean 26.0000% of total sleep. SD 3.2863 %. These changes (in Stage III + IV) slow wave sleep, and in REM sleep) are not significant (p 0.05). From these results it seems that the extended period of sleep consists of Stage I and II slow wave sleep and an increase in transitory arousals.

j) The effect of a loading dose of laevo tryptophan (n = 8).

A loading dose of 5G laevo tryptophan was administered to eight subjects in the group. No evidence of SOREM periods occurred and no significant changes in the latency of the first REM sleep period was noted.

k) Mental activity in sleep.

Number of arousals 16

I. Wakened from REM sleep n = 10.

(a) Reports of mental activity involving fantasy or disorientation 8 (80%)

(b) mental activity denied 2 (20%)

II. Wakened from slow wave sleep n = 16.

(a) mental activity involving fantasy/disorientation 1 (6.25)

(b) mental activity denied 11 (68.8%)

(c) mental activity described as 'thinking' 4 (25.0%)

1) b <u>Sleep in the day n = 13.</u>

All subjects were recorded under the same circumstances as the narcoleptic group.

Number of recordings	=	33
At 12 noon	=	20
At 17.30 hours	=	6
At 19.30 hours	=	7

(a) %OREM periods. None recorded.

(b) Drowsy only. Most subjects were drowsy in the first day recording. 11 instances

(c) Latency to spindles. Mean 7.98 min. frequency preceded by Stage I drowsiness for up to 5 mins.

(d) Duration of sleep. Mean 31 mins. usually Stage II but Stage III was seen on 8 occasions.

(e) REM sleep. On one occasion a 20 min. REM sleep period occurred with a latency of 52 mins. during an evening sleep.

(f) There was no occasion in these recordings when some evidence of at least drowsiness was not present.

<u>Kleine Levin Syndrome n = 3.</u>

(a) SOREM periods. None recorded.

(b) Latency to sleep (d) Usually less than 15 mins. Range 5-42 min. Mean 12.75 min. SD 9.7153 min.

(c) Latency to REM sleep (D). Usually in excess of 65 minutes. Range 61-116 mins. Mean 81.3333 min. SD 14.8956 min.

(d) The amount of sleep. The group were able to sleep a mean of 95.38% of the time available. (SD 2.50).

(e) Periods of arousal. Range 1-6/night. Mean number of periods of arousal/night = 2.8333. SD 2.2088.

Mean time awake = 13.9167 mins.

SD = 10.6127 mins.

(f) Shifts to Stage I or AW/hour. Range 1.33-4.66 shifts/hour.

Mean = 3.0800

SD = 1.1273

(g) Amount of Stage III + IV slow wave sleep. Range 19.6% - 26.8%.

Mean 23.3083% of total sleep

SD 1.9564%.

(h) Amount of REM sleep. 16.3-28.2% of total sleep.

Mean 22.0917%

SD 3.0482%

(i) Extended sleep.

On several occasions all three subjects were allowed to decide when to get up, but with one exception, the amount of sleep was less than 503 mins (95.38% of time available). Subject II complained of hypersomnia and slept 672 mins. (93.9% of time available). On that night latency to sleep (d) was slightly below normal, but latency to REM sleep was normal and the amount of Stage III and IV did not change. The number of arousals and time awake increased slightly REM sleep was not significantly affected and the increase was largely in Stages I and II of slow wave sleep.

(j) Mental activity in sleep n = 3.

When woken from REM sleep n = 5.

(a) Mental activity involving fantasy/ disorientation 4 (80%)

(b) mental activity denied 1 (20%)

When woken from SW sleep n = 7.

(a) mental activity involving fantasy/disorientation	1	(14.3%)
(b) mental activity denied	4	(57.1%)
(c) mental activity described as 'thinking'	2	(28.5%)

(k) Sleep in the day n = 10.

At 12 noon	5
17.30 hours	1
19.30 hours	2

Outcome

(a) no sleep	2
(b) drowsiness only	1

(c) latency to Stage II sleep (D)
Range 5-24 mins. Mean 10.4 mins.

(d) Duration of sleep.
Range 5-36 mins. Mean 22.5 mins.

(e) REM sleep. No REM sleep was recorded in these episodes of diurnal sleep.

Pickwickian Syndrome n = 2.

Male I.

Results of six overnight recordings

1. Delay to sleep (d).

   This was not easy to establish.

   Range 8 - 45 mins.

   Mean 27 mins.

   SD 14.28 mins.

2. Delay to first REM sleep (D).

   Very variable. 105 - infinity (minutes).

   Mean 142 mins.

   SD 26.74 mins.

3. Total sleep time.

   Range 51.4% - 84.4% of time available.

   Mean 71.15% of time available

   SD 11.99%.

4. Stages I + II. Constitutes most of sleep.

   Range 70.4% to 91.9%

   Mean 81.8%

   SD 9.16%

5. Stage III. Very rare. Absent or less than 4% on most nights.

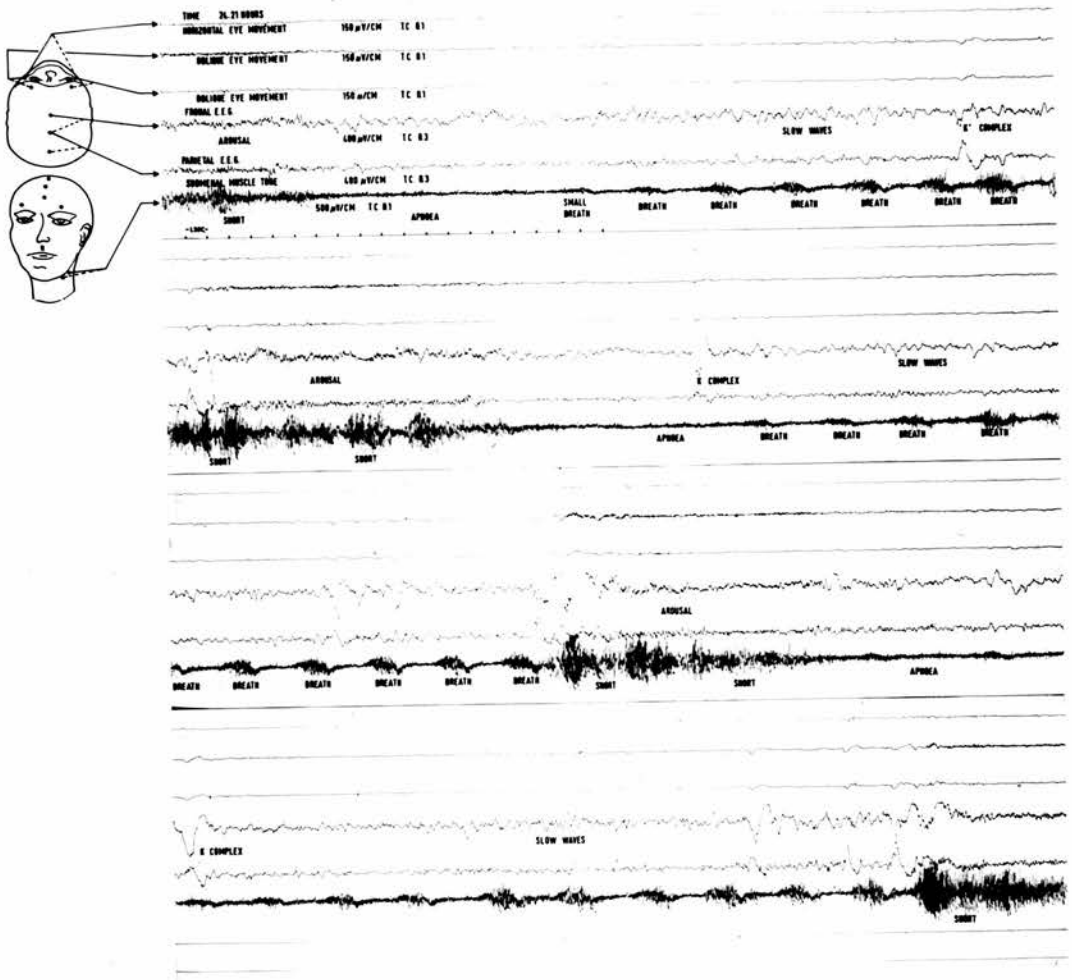
6. Stage IV was never present.

7. REM sleep. Depressed.

   Range 0 - 10.3% of total sleep

   Mean 8.68%

   SD 1.44%



PICKWICKIAN SYNDROME. THE CYCLE OF RESPIRATION SHOWS A QUIET APNEA PERIOD, THEN A FEW BREATHS CULMINATING IN A SNORT WITH MARKED MUSCLE MOVEMENT AND AROUSAL

8. Shifts to Awake or Stage I/hour.

Elevated.

Range 4.33 - 11.1 shifts/hour

Mean 8.92

SD 2.36 shifts/hour.

Sleep shows severe disruption of the cycles of sleep. Drowsiness progressing to Stage I or II is associated with ineffective respiratory movements leading to a period of apnoea of the order of 30-40 seconds. Jerking ineffective respiratory movements often associated with myoclonic like jerks of arms, legs and head lead quickly to arousal or Stage I sleep with many K-complexes. Typically there is a snorting respiration which is extremely noisy and ferocious! Effective respiration allows drowsiness and early sleep to return but apnoea again produces arousal.

Sleep is composed of a series of abortive shallow slow sleep cycles with occasional larger periods at Stage II and rarely Stage III sleep stages. Stage IV was never seen. REM sleep periods usually occurred once or twice a night. The first period was often very short and the second, in the early morning was more prolonged. In REM sleep respiration was quiet and uncomplicated.

Respiration difficulties during slow wave sleep were not influenced by position in sleep or by the introduction of an airway. No evidence of obstruction was noted and cyanosis indrawing of intercostal muscles were absent.

Diurnal sleep

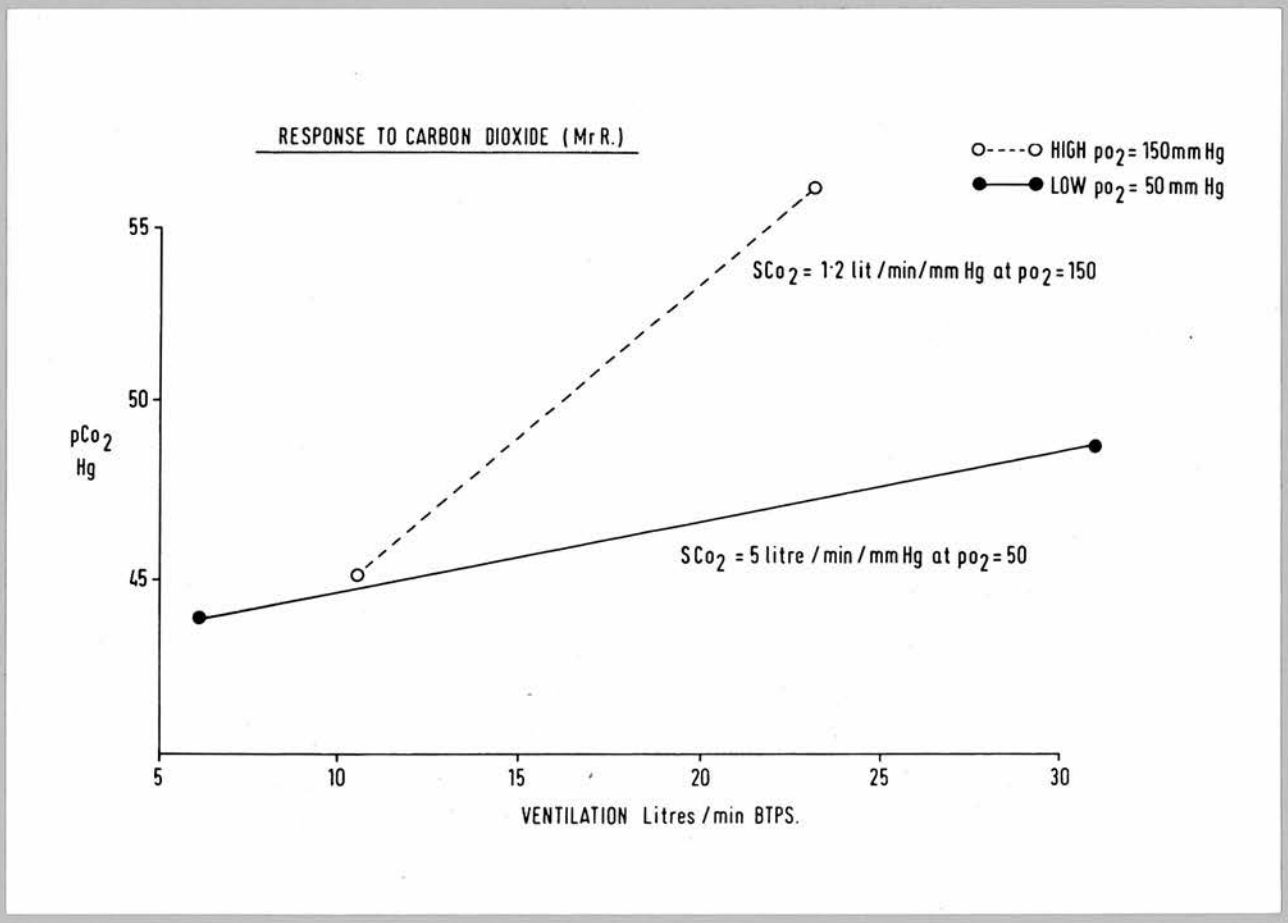
Sleep in day followed same process as at night. Drowsiness (Stage I) was associated with ineffective breathing leading to apnoea for 20 secs or so. Snorting arousal then occurred and the cycle was repeated.

Only short periods of low voltage theta dominant EEG were seen.

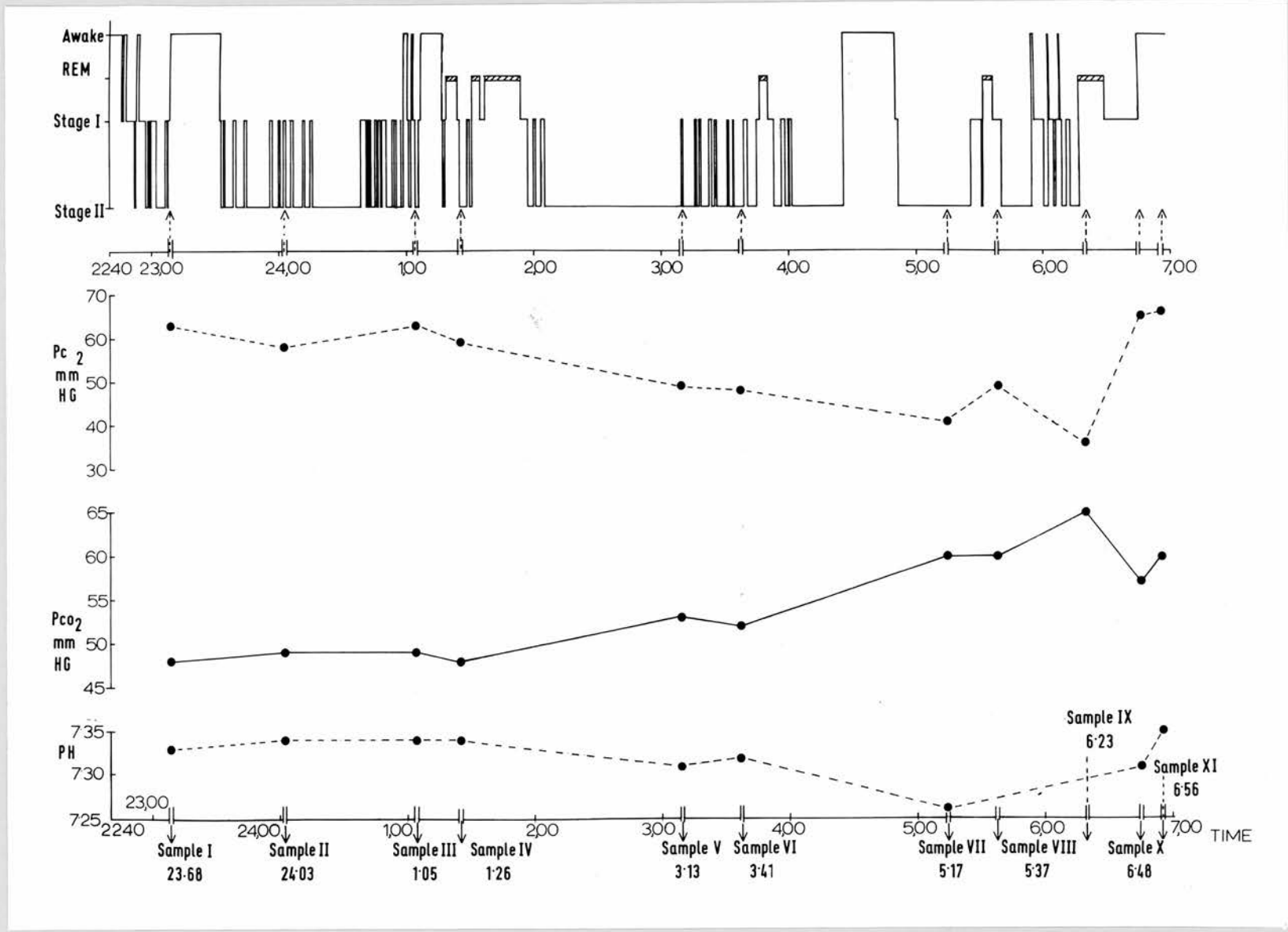
Laboratory investigations (by courtesy of Dr. D.C. Flenley, Department of Medicine, University of Edinburgh).

Ventilation studies were carried out at the department of medicine.

Summary of findings/



THE VENTILATORY RESPONSE TO CARBON DIOXIDE STIMULUS AT TWO LEVELS OF OXYGENATION. SUBJECT M.1.



PICKWICKIAN SYNDROME. NOTE 1. THE LACK OF STAGES III + IV OF SLOW SLEEP
2. THE SHORT PERIODS OF REM SLEEP
3. THE SLOW DECLINE IN pO_2 REACHING A NADIR DURING REM SLEEP at 06.30 hrs.

Summary of findings

Vital capacity was reduced by 1 litre.

Forced expiratory volume (1 second) 2 litres (preduced value 3.3 litres). Breathing air - evidence of mild hypoxia. pO_2 Mm Hq. pCO_2 and pH were within normal limits.

Nocturnal Study

On the night following the insertion of the arterial catheter, arterial specimens were collected at intervals during the night according to the stage of sleep. Details of the time sampling are displayed in the adjacent figure.

With the start of sleep, pCO_2 rose slightly and pO_2 fell. Despite the relatively infrequent samples, it was obvious that pO_2 continued to full and pCO_2 continued to rise.

These changes were more noticeable during the last four hours of the night. The maximal changes were found in the last REM sleep period at 06.00 hours, when a pO_2 of 36 mmHg and a pCO_2 of 66 Hg were present. During this period of sleep despite these immense drives to ventilation, the subject's respiration was normal. The divorcement of hypoxia and hypercapnia to respiration during sleep was in marked contrast to the normal hypoxia drive during arousal which was previously discussed.

Subject M2

Results of three overnight recordings.

I. Delay to sleep (d) is within the normal range

Mean 26 mins.

II. Delay to REM sleep D. Variable.

Range 66-239 mins. No SOREM periods occurred.

III. Total sleep time. Subject slept between 88 and 92% of the total time available.

IV. Stage I + II. This comprise about the whole of the record. 81.7%, 78.6%, 52.4%.

V. Stages III + IV. Only on one recording night was a period of Stage III + IV sleep seen - a late cycle of slow sleep occurred about 0500 hours which put the value of Stage III + IV up from zero to 12%.

OVERNIGHT SLEEP STUDY. SUBJECT M.2.
ESTIMATES OF ARTERIAL pO_2, pO_2 and pH
AT INTERVALS IN RELATION TO SLEEP

VI. REM sleep. The amount of REM sleep was below the low normal range, i.e. 11.6%, 13.1% and 17.4%.

VII. Shifts to Aw/or Stage I sleep/hour. Elevated, 29.3, 7.0, 10.1 shifts/hour.

The typical Pickwickian sleep disturbance was clearly found in this subject. Drowsiness was associated with ineffective respiration and apnea. Continued apnoea resulted in a run of jerking inspirations with myoclonic jerks of the limbs. A large snorting respiration which frequently aroused the subject also restored respiration.

This cycle of events continued almost all night. It resulted in the increase in shifts to Awake or Stage I sleep; the excess of Stages I + II slow wave sleep at the expense of Stages II + IV sleep. Stage of REM sleep was also depressed, but several REM sleep periods were identified in the night at regular intervals.

In REM sleep there were less snorting respirations and at times respiration was noiseless for long periods. No evidence of any airway obstruction was found in sleep in this patient and the snorting respiration was not related to the position of the patient in sleep.

In this patient a cycle of slow wave sleep which contained much Stage IV sleep was noted in the early hours of one overnight record and the snorting respiration was not prominent.

Diurnal record

Essentially no different than the start of sleep at night. No SOREM periods were found.

Sleep consisted entirely of the low voltage Stage I and II of the typical Pickwickian cycles.

Laboratory investigations

Resting awake pO_2 = 65 mm. Hq; pCO_2 38 mm Hq; pH 7.38. Respiratory function tests were all within normal limits. No evidence of airway obstruction or bronchitis. The response to hypercapnia and hypoxia were normal. CO_2 response of 3.8 litres/mm/mmHq. Hypoxia drive was normal.

Sleep study

During nocturnal sleep, initial rise in pCO_2 to/

/to 50 mm Hq and slight fall in pO_2 to 68 mm Hq occurred. Blood gases in this subject remainded within the normal range, throughout the night. The fluctuation in pO_2 and pCO_2 were small and there was no overal effect. Lower pO_2 values were noted during REM sleep periods and there was the elevation of pCO_2 at these times.

DISCUSSION

The sleep studies effectively split the hypersomnia group into three parts:-

1. The subjects showing sleep onset REM periods.
2. Two patients who show a characteristic disruption of sleep, so that little time is spent in any sleep stage and definite sleep cycles are absent or minimal.
3. The remainder who show no disorder of sleep as it can be measured in this study.

1. Subjects showing SOREM periods

These subjects, with one exception are derived from the clinical 'idiopathic narcolepsy' group. The exception is one patient suffering from a post encephalitic hypersomnia. In particular, SOREM periods correlate with patients who complain of cataplexy, or sleep paralysis or hypnogogic hallucinations. This confirms the findings of RECHTSCHAFFEN (1963) and TAKAHASKI, (1963).

Cataplexy, sleep paralysis and hypnogogic hallucinations may be understood in terms of the physiological changes of REM sleep. Total cataplexy was not recorded in this study but in response to my attempts to induce cataplexy I was able to find episodes in the resting record when muscle tone dropped suddenly for periods of one or two seconds, and this was associated with alpha activity in the EEG and occasionally followed by some frontal theta activity. Subsequently patients described feelings of weakness of face or head/

/head muscles but I had no definite proof that these feelings related entirely to the periods of low tone. However other workers (HISHIKAWA, 1965, 1968, SUZUKI, 1966, DEMENT, 1966, RECHTSCHAFFEN, 1967) have described similar episodes and SUZUKI (1966) found that there were occasions when, if the subject did not arouse spontaneously, a full blown picture of SOREM period resulted.

The full significance of these abortive REM sleep changes did not appear until in 1969 I was involved in a study of the effects of mono-amine oxidase inhibitor drugs (AKINDELE, 1970, in press). In sufficient dose (60-90mg) phenelzine obliterated REM sleep but over a period of five or so days. There was then a period when although the eye movements were absent, regular periods of tone abolition still occurred until this was also obliterated. This 'fragmentation' of the various physiological changes of REM sleep certainly lends support to the concept of cataplexy as an early or prodromal feature of REM sleep. In the normal, tone often drops well in advance of any of the EEG or oculographic changes of REM sleep.

Sleep Paralysis

This state was relatively frequently recorded in SOREM periods. Polygraphic changes showed active REM sleep associated with bursts of muscle and movement artifact. Finally movement led to arousal with alpha activity and eye mpvements and blinks.

/blinks. The paradox that the polygraph showed clear changes of REM sleep whilst the subject insisted he or she had been 'awake for hours' poses many problems. Several times the subject claimed to have evidence of events which occurred when they were paralysed, e.g. 'I could hear you talking in the next room and then the door shut' which was in several instances correct.

The explanation lies in the REM sleep state. HISHIKAWA (1965) found that a narcoleptic successfully counted flashes of light during a REM period. In normal subjects, WILLIAMS (1966) showed that REM sleep was flexible as far as responses to stimuli were concerned. Under normal conditions responses were of the same order of those made in Stage III and IV slow wave sleep which made many early workers regard REM sleep as 'deep sleep'. However loading the stimulus with the threat of punishment, raised responses in REM sleep to the level of Stage I and II slow wave sleep.

Perception of the stimulus might be supposed to occur during the short periods of alpha activity which occur in REM sleep after body movements, but several authors have demonstrated that discrimination of stimuli can occur without EEG evidence of significant arousal (WILLIAMS, 1966, OSWALD, 1960, GRANADO,1961).

On many occasions it has been demonstrated that stimuli received during the REM period act on and are incorporated in the on going dream fantasy, often in surprisingly/

/surprisingly sophisticated forms. (BERGER, 1963). Inforporation is in fact demonstrated in one of the dreams from a narcoleptic sleep in the results.

But in the sleep paralysis state the patient seems to be very orientated towards the outside world and there is no evidence that incoming stimuli are incorporated in the mental life, nor are they efficient for some time in producing arousal.

Hypnogogic Hallucinations

Description of hypnogogic hallucinations were usually associated with sleep paralysis during the SOREM period. Patients did not describe them as dreams although there seemed no difference in content between the description of hypnogogic hallucinations and vivid dreams. However the subjects seemed to be strongly orientated towards the surrounding world and saw these visual or tactile experiences as a hallucination, not part of some 'internal' dream process.

The fact that both sleep paralysis and hypnogogic hallucinations occur in the normal subject (GOODE, 1962, LIDDON, 1967), confirms that the physiological changes of REM sleep can on occasion produce these experiences in the normal.

Mental activity

After my experiences I feel surprised ~~at first~~ that an authority associated with narcolepsy for so many years - Bedrich Roch (ROTH, 1969) suggests that dream activity is only/

/only rarely described following narcoleptic diurnal sleep.

However, I think the explanation lies in the circumstances of the SOREM period.

In the normal subject, REM sleep is separated from arousal by a cycle of slow wave sleep which lasts a minimum of 45 minutes (Oswald, 1963). So while the normal may wake from REM sleep, or even occasionally wake from slow sleep and return to sleep into a REM sleep period, there is no occasion when arousal gives way directly to REM sleep. In the SOREM period, a fully developed REM sleep state may commence instantaneously, or REM sleep follows after a few minutes of descending Stage I sleep. From the patient's point of view this poses unusual problems.

The commonest account of mental activity following a SOREM period was a denial of sleep and the explanation that I or a nurse came into the sleep room and adjusted some piece of apparatus. Now this could well have happened - its 'reality' value was high and the subject offered this as evidence of the fact that no sleep had intruded - it was definitely not a dream. If as sometimes happened the mental activity ~~started in~~ was initially plausible ~~state~~ and became more fantastic, This was usually more acceptable to the patient as a dream - ergo, 'I must have slept'.

DEMENT and RECHTSCHAFFEN (1967) had precisely the same experience and were able to illustrate mental activity/

/activity in the SOREM period which the subject could not evaluate in reality terms, as the amount of reality based detail was high.

The lack of reported dreams in the SOREM periods are in marked contrast to the reports of vivid dreams or nightmares in overnight sleep which are frequently reported (DANIELS, 1934, ROTH, 1969). Here the patient seems to have much less difficulty in defining the 'fantasy' nature of the experience.

The SOREM period starts in the reality of consciousness and frequently remains atuned to reality as far as the mental activity is concerned. I consider this the problem of a consciousness/REM sleep continuum. There is a further problem to the SOREM period - a disorder of omission. While the patient is involved in REM sleep events may occur in the outside world which he may not perceive. One patient (M1) a motor mechanic frequently had narcoleptic attacks while lying under a car. On arousal he often found his tools missing and concluded they had been stolen. Investigation revealed that a colleague had 'borrowed' them while the patient slept and usually insisted that he had acknowledged the loan of the article with a grunt or mutter!

If the explanation of cataplexy, sleep paralysis and hypnogogic hallucinations lies in the REM sleep state, is the SOREM period unique to idiopathic narcolepsy with cataplexy? The latency of the first REM periods is/

/is normally in excess of 45 minutes. Even in states of severe sleep loss, when allowed to sleep, subjects initially spend more time in slow wave sleep than in REM sleep, so slow wave sleep takes precedence, (OSWALD, 1962).

In the recovery sleep following several nights of selective REM sleep deprivation (DEMENT, 1960) the latency to first REM sleep became very short but only rarely did SOREM occur. These subjects did not develop cataplexy.

Abnormally short latency to first REM sleep has been found in drug withdrawal states (OSWALD, 1965, EVANS, 1968) in early delirium tremens (EVANS, 1968, GROSS et al. 1966) and in some normal subjects (AKINDELE et al. 1970, MARON, 1964) LANE (1965) describes isolated patients with a heterogenous group of illnesses (post encephalitic Parkinsonism, schizophrenia, catatonic illness and severe insomnia) in whom SOREM periods or short latency to first REM sleep were encountered but this observation is not general in such conditions.

To the present time however SOREM periods occur only consistently in narcoleptic patients with cataplexy.

This explanation of the symptoms of narcolepsy raises several problems.

1. In the several published investigations of idiopathic narcoleptics (RECHTSCHAFFEN, 1963, TAKAHASHI, 1963, HISHIKAWA, 1965, 1968, SUZUKI, 1966, ROTH, 1969, DEMENT, 1967) the frequency with which SOREM periods were recorded varied/

/recorded varied from 40-80% of occasions.

In many of these experiments a routine EEG recording situation was used to record sleep and it is noticeable that SOREM periods were most frequently recorded by SUZUKI (1966) who recorded overnight sleep and less frequently by HISHIKAWA (1968) and ROTH (1970) using EEG laboratory conditions.

In my studies I soon realized that several factors led to 'false negative' results. In particular, (a) anxiety and novelty were very effective in depressing SOREM periods and even a stranger in the laboratory was enough to alter the sleep of some subjects. Anxiety and novelty has been shown to affect the sleep - depressing REM sleep in particular in first nights in the laboratory (MENDELS 1967) and some subjects commented that the negative result correlated with high anxiety levels in their lives. Patient F6 also was going through a difficult divorce process and could predict fairly well whether she would have a SOREM period on a given night in relation to her anxiety level that day, (b) the next difficulty was the problem of a prior sleep. Subjects who needed to travel by bus or train to reach the laboratory frequently had curtailed or abortive SOREM periods and on phenomenological grounds it appeared that a sleep episode within two hours of a recording usually produced a negative result, (c) false negative results were more frequent when subjects were taking sympathetico mimetic drugs, (d) finally, it also became clear that subjects' testimony as to whether/

/whether a prior sleep attack had occurred was unreliable, as sleep episodes were observed to occur in the ward and even while electrodes were being attached, which were denied by the subject.

Minimizing these reasons for false negative results does not however entirely ensure that every patient in the clinical idiopathic narcolepsy category will show SOREM periods. Each investigator has a small number of cases who fail to show SOREM periods. Normally these subjects are found to show evidence only of sleep attacks, and cataplexy is not admitted. However it is well recognised (DANIELS, 1934, ROTH, 1969) that cataplexy may follow sleep attacks by many years. Can one say that such 'independent narcoleptics' (ROTH, 1969) are larval states of narcolepsy or merely very mild narcoleptic disorders? If this were so it could be argued that at this stage in the process of the disorder they only show rare or abortive SOREM periods. However no-one has shown this to be the case so far although it has been possible to follow suspect patients for up to seven years, no positive support for this view has emerged.

In my series, one patient who reported only sleep attacks, was found to have SOREM periods. Further discussion later revealed that he had been aware of feelings of weakness associated with laughter or anger but had learnt to avoid the provocative situation so that it was no longer any problem as a symptom. As this had happened many years before, he/

/he denied any symptoms of cataplexy at the first interview.

My experience with narcoleptic patients in fact makes one rather doubt the assertion by other workers (DEMENT, 1966) that it was clear whether a given patient had experienced cataplexy or not. This is thae only of total or severe partial cataplexy, but mild feelings of weakness are less easily elicited and less meaningful to the patient.

2. Even if the patient does not have SOREM periods, there is no doubt that patients with idiopathic narcolepsy are 'drowsy' people who sleep readily whenever there is a suitable opportunity.

Thus it can be said that narcoleptics show two types of sleep attack. SOREM periods are intrusive and patients often call them irresistable. SOREM periods can occur too when there is a 'lull' period in the day, but frequently in such circumstances for example where normal people may also feel drowsy, the narcoleptic may go into slow wave sleep.

This easy entry to slow wave sleep may account for the frequent complaint of narcoleptics that they suffer from extended sleep and prolonged sleep. Further evidence of this disorder of slow wave sleep is that narcoleptics may be considerably helped with symptoms of cataplexy or sleep paralysis when given drugs which depress REM sleep, e.g. imipramine (HISHIKAWA, 1965, 1968) but continue to complain of sleep attacks. Drugs which both depress REM sleep/

/sleep and incfease vigilance, e.g. amphetamine, are more generally affective.

The conclusion is that idiopathic narcolepsy with associated symptoms is due to a disorder of slow wave sleep. However cases of independant narcolepsy show only a disorder involving the production of slow wave sleep (ROTH, 1969).

Theories of narcolepsy

At the beginning of the exploration of sleep or narcoleptic patients, the SOREM period explanation of the disorder was very attractive. It posed several problems.

1. Was SOREM sleep an expression of an increased demand for this type of sleep?

In the first overnight study (RECHTSCHAFFEN, 1963) of the narcoleptic patients, the amount of REM sleep was no different from the normal control group. However, this comparison was made on first night sleep in the laboratory, which may account for the low normal values in the series (mean 18.8%).

SUZUKI (1966) found increased levels of overnight REM sleep in his group of narcoleptics (mean 30%). He did not find that the excess REM sleep was entirely accounted for by SOREM period and considered that his group of narcoleptics were more severely ill than those investigated by Rechtschaffen. Suzuki does not make it clear how many first nights in the laboratory were included in the study and how much a given individual contributed to this data. Suzuki also accepted subjects in this study who had been off drugs/

/drugs for not less than four days. A drug withdrawal REM sleep rebound would not have subsided in that time (OSWALD, 1963).

In this study the amount of REM sleep in the narcoleptic group (n = 15) was significantly greater than that of the control group, matched for age and sex. However removal of the SOREM period from the total REM sleep removed this difference.

The evidence is that SOREM period is not an index that there is a general and excessive demand for REM sleep as may be seen in a drug withdrawal state.

2. Was the SOREM period due to a degree of REM depression which occurred because of the appearance of excess slow wave sleep in the day?

The experiment of sleep satiation in which a narcoleptic was allowed to sleep ad lib and therefore could ensure that the necessary 'balance' between REM sleep and slow wave sleep could be maintained, had SOREM periods on two occasions after a few hours of arousal.

Further several narcoleptic patients recall that under tense and demanding conditions they had managed to prevent any sleep attacks for up to 12 or 24 hours on isolated occasions. This invariably led to a great demand for sleep and one subject (M1) suffered cataplexy after such a period. He once drove to London to visit his father in his terminal illness. The car broke down several times and the drive was very anxiety provoking. On arrival he greeted his sister/

/sister and had a total cataplectic attack, falling at her feet.

3. Is the SOREM period due to precocious 'triggering'?

The appearance of REM sleep periods in the night in normal subjects is often abrupt and lends support to the concept of a 'trigger' which sets off the neurophysiological mechanisms of REM sleep. JOUVET (1963) has described the pontine centre which he suggests is a trigger zone which is connected caudally with the inhibitory extra pyramidal system relay nuclei at the lower end of the reticular formation, and superiorly with the limbic midbrain circuit and the geniculate body, occipital cortex circuits. Suitable electrical stimulation in this area can trigger REM sleep during slow wave sleep periods and ablation of this centre in cats prevented the appearance of REM sleep.

However, Jouvet also found that after one period of stimulation, a delay of 20 minutes or so was needed before further stimulation could trigger a period of REM sleep. This evidence suggested that a chemical transmitter was involved in the production of the REM sleep and stimulation exhausted the supply of neurochemical which required time to build up further.

4. In idiopathic narcolepsy a disorder of the circadian pattern of sleep?

Various hypotheses have been drawn up to explain the circadian arrangement of arousal/slow wave sleep/REM sleep in the normal subject.

RECHTSCHAFFEN and DEMENT (1967) suggest that arousal exerts an inhibitory effect on both slow wave sleep and REM sleep. Arousal manifestly depends on a supply of incoming sensory information which will reinforce the tonic ascending discharges of the upper reticular formation. Other influences, stimulation of carotid receptors, distension of hollow viscus, barometric pressure could all have depressing effects on the reticular formation and in this way promote slow wave sleep. Equally there is good evidence of the relationship of cerebral cortex and the non specific arousal system during sleep which allows for selective control of incoming sensory information and can promote sleep.

During arousal the altering effects of the upper reticular formation is not damped by the cortex or any midbrain influences. Stimulation of the mid pontine region ~~which~~ in aroused cats, fails to elicit REM sleep as it can do when the cat is in a slow wave sleep cycle (JOUVET, 1965). This evidence would support Rechtschaffen's theory that in the normal arousal is inhibitory to the REM sleep mechanism.

Using this model it is further necessary to hypothesize that the inhibitory effect of arousal is greater on REM sleep than on slow wave sleep under normal circumstances. This ensures that while slow wave sleep can arise contiguously with arousal, REM sleep can only occur after a period of slow wave sleep. This model is compatible with many conditions in which the pressure of REM sleep is increased.

REM sleep fluctuates in relation to the menstrual cycle (HARTMANN, 1966) and in pregnancy (PETRE-QUADENS, 1968). Despite increases in these conditions of the order seen by SUZUKI (1966) in his narcoleptics and in some patients in this study, there is no evidence of SOREM periods in neonates or during pregnancy.

In drug withdrawal states (EVANS, 1968) the latency to REM sleep is very short at times in nocturnal sleep and it is possible that during frank delirium tremens REM sleep can intrude into the day (GREENBERG, 1967, GROSS, 1966). Still while patients in alcoholic withdrawal delirium may be experiencing hypnogogic hallucinations, no evidence is available that they suffer from cataplexy. So there is no experimental or clinical parallel to SOREM periods.

However, this rule of precedence can be seen to break down occasionally in normal sleep. Spontaneous arousal occasionally occurs from a REM sleep period and after a brief but definite period of arousal, REM sleep recurs. At other times times arousal occurs from slow wave sleep and after a definite period of arousal REM sleep develops rapidly. Such examples are not common and it must also be accepted that DEMENT (1965) was able to restrict REM sleep greatly by waking his subjects after a short period of REM sleep. On their return to sleep, slow wave sleep developed.

Accepting the inhibitory effect of arousal differentially on slow wave sleep and REM sleep it can be argued that the/

/the idiopathic narcoleptic suffers from an inadequacy of this inhibition which allows the ready development of slow wave sleep but in particular allows precocious triggering of REM sleep.

In the normal, REM sleep can only be triggered during slow wave sleep and there is a surprisingly regular relationship between the two stages which several workers allude to as the 90 minute REM sleep cycle (HARTMANN, 1968).

As far as the alternation of slow wave sleep/REM sleep is concerned there are two possible hypotheses.

GLOBUS (1966) proposed that REM sleep may be time locked as a ripple on a circadian pattern, with the possibility that it may be represented in the day by time linked events at intervals of 90 minutes, which is the mean inter REM sleep period during the night (OSWALD, 1970). Logically this might be expected to promote SOREM period episodes in narcoleptic patients at regular intervals in the day.

Inspection of sleep charts which were kept for long periods by some of the narcoleptic subjects does not suggest that REM sleep attacks cluster around mean intervals of 90 minutes but as yet this data is insufficient to test this interesting hypothesis adequately statistically.

However, in this study it was clear that SOREM periods did not occur if the subject had suffered a sleep attack within two hours of the start of the recording, and many narcoleptic subjects relate their attacks to around/

/around meal times which are often at 180 minute intervals.

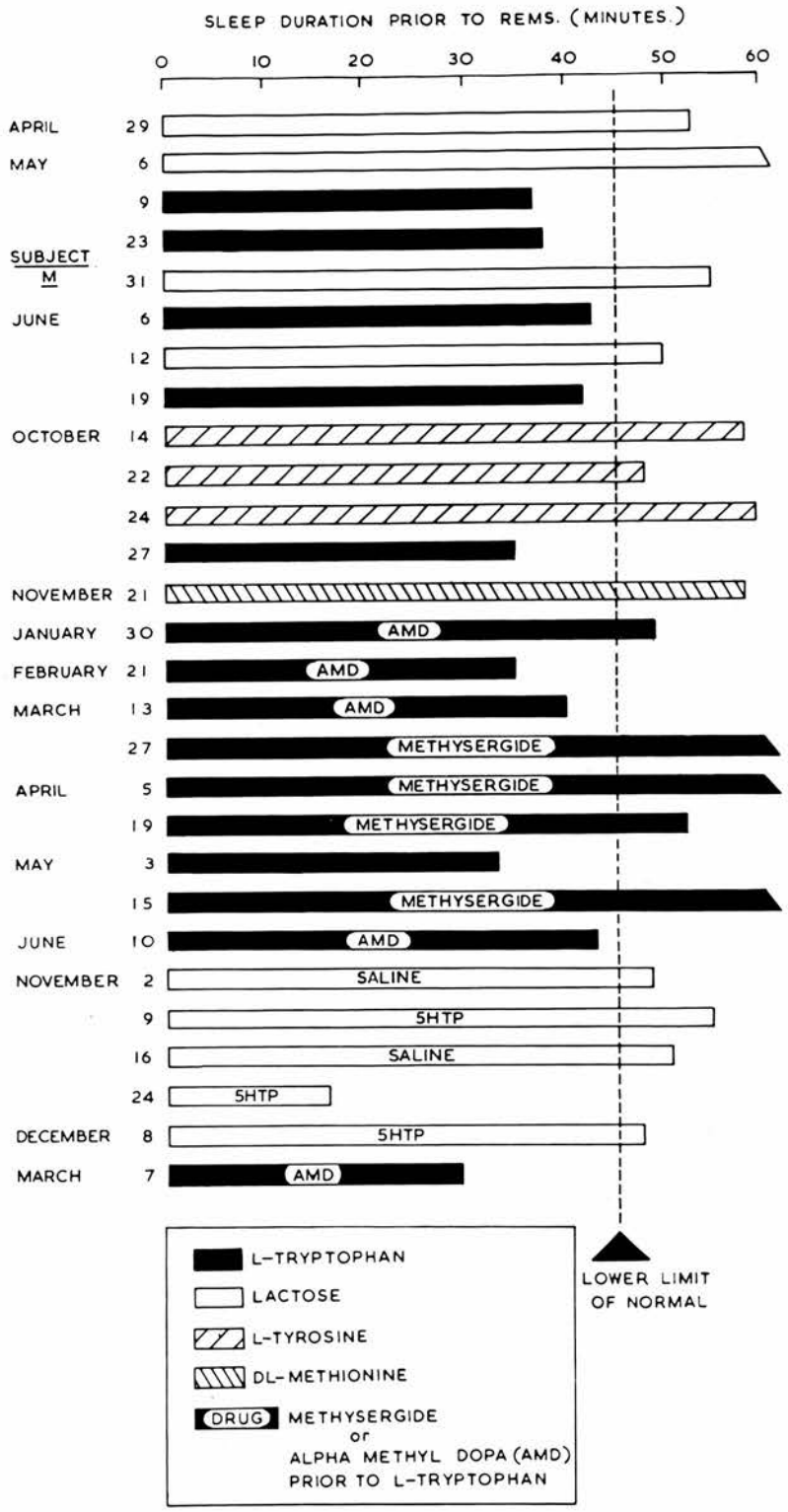
MARON (1964) in a study of napping in the day found the latency to REM sleep was longer in the evening period than in the afternoon which was considered to indicate that the triggering of REM sleep at different levels at these two points in the day. LEWIS (1969) in our laboratory found the latency to REM sleep was unmeasurable as the subjects never slept long enough to reach a REM period in diurnal sleep, which is more in agreement with the control group in this study when they slept in the laboratory in the day.

The alternative hypothesis (DEMENT, 1963) based on the REM sleep depression and rebound experiments, is that REM sleep is triggered by a neurochemical transmitter which accumulates during slow wave sleep and initiates REM sleep when it has reached a sufficient level and is then used up in the ensuing REM sleep period. This theory is of greatest use in the explanation of the 'rebound' effects after REM deprivation experiments (DEMENT, 1963) and after the effects of hypnotic drugs (EVANS, 1968). In keeping with the hypothesis, a positive correlation exists between REM sleep and slow wave sleep and in a previous experiment (LEWIS and EVANS, 1968) a regression equation was constructed from the records of 80 normal subjects which related REM sleep to the total sleep time. A similar relationship of REM sleep and slow wave sleep has been shown by EPHRON (1966) and VERDONE (1968).

Objection to the concept that REM sleep is dependant on prior slow wave sleep arises on several fronts. A subject can on occasion wake from slow sleep in the night and after a wakeful period return to sleep and enter a REM sleep period. Thus REM sleep can be divorced from prior slow wave sleep and wakefulness has not apparently destroyed the neurochemical trigger which it is suggested is needed to initiate the REM sleep period.

Also if the demand for REM sleep is exceptionally high REM sleep seems to be able to intrude to the extent of producing SOREM periods or even some REM sleep activity in the day. (GREENBERG, 1967, GROSS, 1966).

If the initiation of REM sleep is dependant on a neurochemical accumubating in slow wave sleep, then the SOREM period must be due to the accummulation of this transmitter during arousal, as SOREM periods occur after wakeful periods in narcolepsy. Thereafter the trigger mechanism appears normal as the ensuing slow wave sleep/REM sleep cycle is within normal limits. This does not suggest that narcoleptics are excessively sensitive to the level of the neurochemical, or REM sleep is triggered by small accummulations of the transmitter. Attempts have been made to identify this neurochemical transmitter. Neurochemicals are involved in the production of REM sleep. The most complete system experimentally derived to understand the alternation of slow wave sleep/REM sleep has been advanced by JOUVET (1967).



ORAL L-TRYPTOPHAN SHORTENS THE DELAY TO REM SLEEP (D) SIGNIFICANTLY. THIS EFFECT IS BLOCKED BY A SEROTONIN ANTAGONIST (METHYSERGIDE)

There is much evidence that monoamines are involved and on neuropharmacological grounds Jouvet presented evidence that catecholamines were the key transmitter substance in the initiation of REM sleep while serotonin (5.HT) was involved in pathways promoting slow wave sleep in the cat.

It is difficult initially to reconcile these findings with the clinical experiments in narcoleptic patients. Sympathetico mimetic drugs have been shown to be both strong depressors of REM sleep but also disrupt the contihuity of slow wave sleep (RECHTSCHAFFEN, 1964, OSWALD and THACORE, 1963, BAEKELAND, 1966). Also in normal subjects it is possible on occasions to shorten the latency of the first REM period with a loading dose of laevo tryptophan (5G) (OSWALD et al. 1966). In this study narcoleptics proved to be extremely sensitive to the effects of l-tryptophan which significantly increased the length of the SOREM period and also promoted vivid dreams and nightmares. The effect of the tryptophan load was successfully antagonized by amphetamine, methyl phenidate and imipramine, but the effect of a specific serotonin antagonist, methergiside (Deseril) while initially encouraging failed to significantly block the REM sleep enhancing effect of l-tryptophan.

It was significant that l-tryptophan was not effective in altering the REM sleep over the rest of the night and no significant changes in latency to the next REM period ~~or an~~ increase in the total REM sleep was observed.

In an attempt to investigate whether there was evidence of a disturbance of monoamine metabolism, samples of cerebrospinal fluid obtained after a mixing procedure to ensure that the specimen contained ventricular C.S.F.,were examined for the metabolites of the monoamines. These were within normal limits which was confirmed by the work of GUNNE (1966) who found that the C.S.F. content of 5-hydroxyindolacetic acid was normal in their narcoleptics. Further these workers showed that the urinary excretion of naoradrenaline, dopamine and vallinyl mandelic acid were also within normal limits in narcoleptics. No altering effects were found after administration of intravenous dopa.

The apparent paradox in these results and the investigations of JOUVET (1967) may be explained in that there are likely to be species differences which do not allow free generalization of concepts from the cat or rat model to man, and it is also likely that in relation to dose/kilo body weight the work done on the cat is not compatible to work on man as the higher doses are not ethically justified.

But the tryptophan sensitivity of the narcoleptics is not only a potentially useful test of the diagnosis of idiopathic narcoleptic but an illustration of the fact that SOREM periods may be influenced by dietary factors. Tryptophan loading illustrates the sensitivity of the triggering mechanism for narcolepsy SOREM periods.

To date the neurophysiological/neurochemical explanation/

/explanation of SOREM periods in narcolepsy lies in hypothesis that in narcolepsy there is a dysfunction of both the REM sleep production system and in the slow wave sleep production system, neither of which is sufficiently antagonised by wakefulness. The neurochemical trigger mechanism of REM sleep, usually only operative during slow wave sleep, is effective during arousal and causes REM sleep periods to intrude into arousal or to take precedence over slow wave sleep at times. Thus the narcoleptic may suffer from 'attacks' of REM sleep and also periods of slow wave sleep in the day and show SOREM periods at night.

Two other symptoms of narcolepsy are related to REM sleep. DEMENT (1967) showed that in cats where REM sleep can be kept at a low level over long periods, the cat showed an increase in drive. Appetite and weight increased, and aggression and sexual activity were also increased. Weight gain and appetite increase was also found in subjects and depressed patients in whom REM sleep had been seriously depressed or obliterated with monoamine oxidase inhibitor drugs (AKINDELE, et al. in press).

This further suggests that a connection exists between REM sleep and appetite and other drives. It is tempting to explain these changes in terms of hypothalamic or limbic system activity but no evidence of this is present in these studies of narcoleptics.

However, another symptom - the complaint of disturbed sleep and vivid dreams/nightmares, so often made by narcoleptics (DANIELS, 1934, ROTH, 1970) was more clearly understood in this study.

To my surprise, the narcoleptic group failed to show evidence of increased awakening or arousals, and the shifts to Stage I slow wave sleep were within normal limits. The amount of Stage III and IV slow wave sleep was also increased and the evidence as a whole was that on these measures narcoleptics may sleep as well, if not better than controls. The subjective complaint of disturbed sleep was however understandable in the frequency with which vivid dreams or nightmares were reported in the group. Frequently these reports arose when patients woke from SOREM periods but complaints also arose from REM periods later in the night.

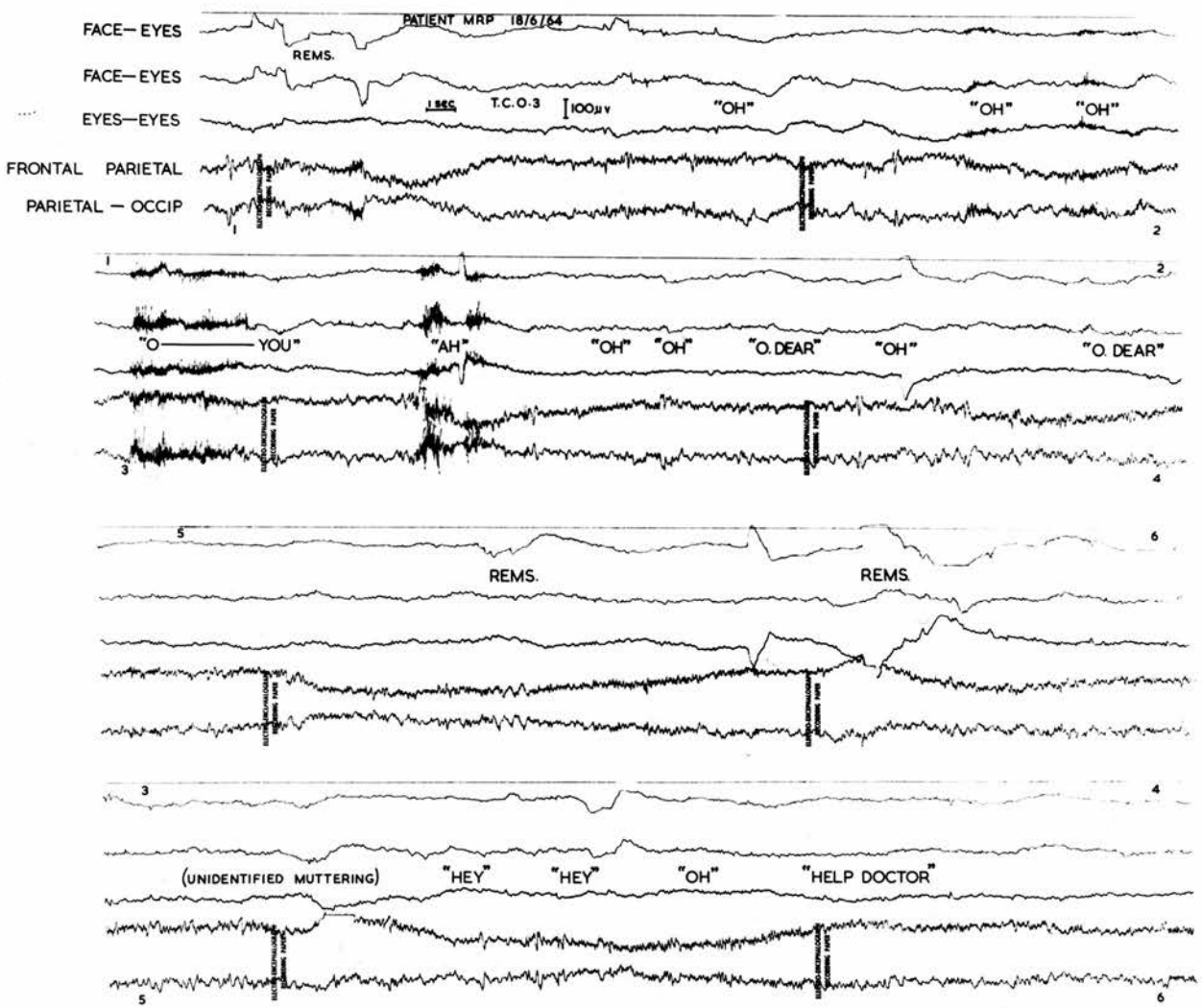
Tryptophan loads frequently produced prolonged and intensive SOREM periods with such active eye movements that many tryptophan records could easily be distinguished on visual inspection from control records of the same subject. If subjects woke from this SOREM period or on the isolated occasions when they shouted from the REM period, accounts of vivid dreams and nightmares emerged.

The subject in Fig. dreamed of being tortured by many red hot steel needles driven into his body. This subject (M1) had been admitted to hospital because of a paranoid illness originally thought to be due to abuse of/

/of amphetamine, methedrine and methylphenidate. Further investigations failed to substantiate the question of abuse and stopping sympathetico mimetic drugs failed to influence the patients paranoid delusions. A diagnosis of schizophrenia was considered likely. However over a period when the sleep of this subject was being recorded, nightmare material which emerged in the laboratory at night and was correctly identified by the subject as a 'dream' was represented by the subject to his own doctor in the day as a delusion. He accused the nightnurse of assaulting him at night by driving in hot needles into his body, and on another occasion after a nightmare in which he related being forced by masked captors to eat a meal he knew to have been poisoned, he accused his ward doctor of placing poison in his food. Frequently the content of the nightmare could be understood as arising from the sleep laboratory situation.

At the time of this recording we were using a skin burr - a small device to prepare skin for electrodes and this was hot and pressed on to skin. Also tryptophan loads were bulky and taken with water. Subjects were told it was an extract of first class protein and many joked that they would prefer to eat the protein directly.

On another occasion, a subject (M2) discovered that the hospital mortuary was in an adjacent building. Several nights later, after a tryptophan load, he dreamt that a skeleton hand entered the partly open window, and taking/



FIRST FULLY RECORDED NIGHTMARE. SOREMP PERIOD WITH INTENSE EYE MOVEMENT. AFTER 5G TRYPTOPHAN. I WROTE DOWN ON RECORD AS SUBJECT SHOUTED

/taking the long electrode cable lead and wound it around his neck, began to choke him. On this occasion, this subject who often rotated in bed in a clockwise direction had in fact wound the electrode lead around his neck.

The frequency of disturbing dreams may be the prime factor in the narcoleptic's complaint of poor quality sleep. However, it may also be the factor responsible for the paranoid illnesses associated with narcolepsy. Many of the described cases were reported to have vivid and distressing dreams (BROWN, 1908, DANIELS, 1934) and all subjects suffered from cataplexy. The reality problem connected with SOREM periods has been discussed and here the question is how the individual patient can defend himself against the invasion of fantasy connected with REM sleep. Provided this fantasy can be excluded from consciousness or labelled as a dream, it does not disturb the individual, but when reality testing is difficult and a question of belief in the fantasy arises, psychiatric disturbance is imminent. However, it must not be doubled that amphetamine contributes to a paranoid state in some patients and there is no reason why schizophrenia and narcolepsy may not co-exist in individual patients.

Narcolepsy and Epilepsy

There no longer seems any reason to specially associate these paroxysmal disorders. Obviously individual cases may be found in which both disorders coexist e.g. F13 in this series but there is no evidence that epilepsy can lead/

/lead to SOREM periods. In fact there is some evidence that anticonvulsant (epanutin) depress REM sleep (COHEN, 1968).

Symptomatic narcolepsy

Only one patient in this group F1 a post-encephalitic showed any signs of SOREM sleep. She complained of occasional cataplexy and the polygraphic data suggests that in her case the encephalitic lesions had been so placed as to disturb the REM sleep producing system.

The remaining patients were essentially drowsy and slept easily although the delay to spindle sleep was usually within the range for normals. In fact one case (M2) slept badly with much arousal and little Stage III and IV sleep, although REM sleep was well preserved.

The patients in this group otherwise illustrate that a variety of cerebral damage - patching diffuse, basilar and frontal in this group, all have the effect of promoting apathy and drowsiness.

On clinical grounds the only reasons for considering them as sympathetic narcoleptics was that they complained of sleep attacks. However, such attacks can be seen to be due to an increase in the general level of drowsiness rather than an 'attack' proper. The only subject in the group in whom a diagnosis of symptomatic narcolepsy may be justified was F1, a post encephalitic patient. However, patient M4 also claimed occasional cataplexy although the account was extremely vague. Cataplexy has been recorded in patients with cortical lesions of the frontal lobes (ETHELBERG, 1950)/

/(ETHELBERG, 1950) and his patient had extensive bilateral frontal lobe lesions. However no SOREM periods were recorded in this case.

Non-specific hypersomnia

Sleep studies revealed little about this heterogenous group. No SOREM periods occurred and none of the measurable dimensions of sleep reflected any change. As a group they confirmed that they were able to sleep well although the older patients in the group were less able to sleep either promptly or continuously. Arousal during the night was not significantly depressed and when allowed to extend that sleep the increase was moderate and chiefly in the form of Stage I and II slow wave sleep. The principle abnormality in this group of patients was that when aroused transitorily in the morning they frequently allowed themselves to return to sleep. On entry to the sleep cubicles to remove electrodes they usually requested to be allowed to continue sleep as they were still tired! Unfortunately during this study I was not able to test arousal thresholds with these subjects but casual testing suggested that 'K' complexes were easily elicited and it was quite possible to arouse the subject by tapping on the microphone to the sleep room. Unlike the normal subject they simply 'turned over and went back to sleep'.

An interesting exception (F5) did have one night of increased pressure to REM sleep (delay (D) 38 mins, REM sleep percentage 34.4%). This was the second laboratory night/

/night and in the light of the history of ataxia and of the fast activity previously noted in her resting EEG it was decided that this increase was due to drug withdrawal. It was subsequently proved that she had been addicted to meprobamate (Equanil).

The evidence from diurnal sleep studies in this group was simply that idiopathic hypersomnia patients can drowse very frequently and on other occasions develope slow wave sleep. However there was no evidence of any REM sleep disorder.

These sleep studies merely suggest that hypersomniacs are individuals who can readily develop slow wave sleep whenever the circumstances allow. It may be that in they suffer from an inadequacy of arousal to antagonize slow wave sleep but there is no evidence of a disorder of arousal in this study.

Kleine Levin Syndrome

The polygraphic studies of the sleep of these patients failed to confirm any abnormalities. SOREM periods were absent and the measurable dimensions of slow wave sleep were within normal limits.

In general, like the idiopathic hypersomnia group, these patients showed that they could sleep readily when the occasion allowed.

The sleep of MII who was complaining of current hypersomnia, was not remarkable. The increase in sleeping/

/sleeping time was entirely due to an extension of Stage I and VI slow wave sleep.

No evidence is available to suggest that these subjects are less arousable than normal and in fact during most of the study these patients made less complaint about getting up than did the idiopathic hypersomnia patients.

Clinical data

Bringing together this data has altered many of my impressions accumulated during the collection of patients in the study. Although, for example there seemed to be an excess of female subjects, the sex ratio is nearer to 3 male to 2 female noted by SOURS,(1963). Whether this is a true sex difference remains in doubt as it still seems likely that male narcoleptics may have greater social reasons for complaint than female patients have (HEYCK, 1957). Certainly publicity in this study brought letters from more female narcoleptics than male subjects and for this reason I feel that any incidence figures on sex ratios in relation to narcolepsy must be treated with great caution. This impression was further confirmed when in correspondence with Allan Rechtschaffen (personal communication 1969) he related that on several occasions he had diagnosed narcolepsy on clinical grounds when on social occasions people related to him their sleep troubles. Rechtschaffen suggested that the disorder is frequently underdiagnosed as subjects do not always complain, doctors may not recognise the disorder as significant and/

/and the fact that sleep paralysis, hypnogogic hallucinations and the weakness most people note in themselves when laughing are accepted as normal phenomena. He advertised on one occasion when requiring narcoleptic subjects for research simply stating "wanted for research studies; persons with narcolepsy". In the first week 40 calls were received of which approximately two thirds presented unambiguous narcoleptic symptoms.

The most pressing reason for establishing the incidence of idiopathic narcolepsy is the current difficulty with drug addiction. Unless a more appropriate treatment than a sympathetico-mimetic drug is developed, amphetamine and methyl phenidate will need to be prescribed regularly for these patients. The addictive properties and abuse of these drugs especially amphetamine may lead to its withdrawal from the pharmacopea, and before this could be justified it would be important to establish the demand for the drug in the treatment of narcolepsy.

The data relating to symptoms and their combination is in general agreement with that of SOURS (1963), YOSS and DALY (1957) and GOODE (1962). Sleep attacks with cataplexy remains the most frequent combination of complaints while sleep attacks with sleep paralysis or hypnogogic hallucinations are less frequent. No isolated cases complaining of sleep paralysis were found in this series and the full tetrad of symptoms occurred approximately once in every five narcoleptics.

Associated sleep symptoms were frequent in this group of patients. Six patients for example recorded that they had on occasions slept for more than 24 hours, and thirteen patients complained of excessive length of overnight sleep. These complaints emphasise that many narcoleptics have symptoms of hypersomnia. One interesting finding was that patients often stated that the duration of sleep attacks was of the order of 10-15 minutes and as the study continued I discovered that many subjects described that they fell asleep at night extremely rapidly and woke feeling they had slept for a long time only to find 10-20 minutes had elapsed. One subject (M10) made the spontaneous observation that in this period of time he was dreaming. His wife had noted that in this precipitate sleep he grimaced excessively, muttered occasionally and sometimes talked of traumatic experience. She actually asked me in an interview why her husband should have a penile erection during this sleep.

I therefore began to ask subjects if they had this experience at night, i.e. an abrupt 10-15 min sleep which seemed longer and was associated with dreaming. The presence of this experience is proof of idiopathic narcolepsy as the polygraphic studies have confirmed. This clinical question depends of course, on the subject's arousal, which certainly does not occur regularly, so that the subject's lack of recognition of this phenomenon does not rule out the possibility of an idiopathic narcoleptic diagnosis, but it has proved helpful in establishing the diagnosis.

No study of hypersomnia has enabled the researcher to be emphatic on the question of a genetic basis for the disorder. Retrospective studies offer the advantages of large numbers of subjects but tracing them and obtaining accurate family histories is a difficult task. Prospective studies generally find much greater difficulty in mustering sufficient patients to offer enough genetic data. Examples of familial cases exist (DALY, 1959). Despite this epidemiological difficulty, most studies present some evidence of a familial basis for symptoms (NEBSIMAL, 1958) frequently that some first or second degree relative suffered from some problem of extended sleep or had sleep attacks. KRABBE (1942) described a family considered to be narcoleptic. Inspection of the description of patients reveals that it is more likely that these patients suffered from a familial form of the Pickwickian syndrome. In the individual case, complaints are most difficult to assess, but on occasion a narcoleptic noted that a first degree relative also suffered from cataplexy which makes for a more satisfactory presumptive diagnosis. In this study the sister of F6 had complained of sleep attacks and cataplexy but was now resident in New Zealand so that it was never possible to examine her sleep. SOURS (1963) described nine patients who had some family member with narcoleptic symptoms, and IMLAH (1961) described narcolepsy in identical twins. If there is any genetic basis for the disorder it is only possible to see/

/it in terms of a dominent gene of low and orregular penetration, (DALY, 1959) but for practical purposes when confronted as does happen in discussing narcolepsy with a patient, with a question on the heredity of the disorder, I emphasize the inadequate evidence of a genetic basis.

Estimates obtained from patients about the onset of symptoms indicate the recognition of symptoms is uaually in the mid adolescent period. However further discussion frequently reveals that the patient is usually dating the disorder to some definite event, usually an example of a time when the sleep attack was incongruous or cataplexy occurred causing embarassment. The original event is often located to sleeping in an examination or in class. Frequently over a number of visits to the laboratory, patients recall earlier and earlier evidence of sleep attacks or cataplexy which was however less prominent or regular. My impression is that many narcoleptics date their symptoms from the time in life when in general they became more aware of themselves - adolescence. This question of the awareness of symptoms is a problem in diagnosis. Most authors seem satisfied that patients recognise cataplexy as a discrete event and are therefore sure of its presence or absence. A great deal of the time this is true, but as the analysis of the cataplexy incidents shows, on most occasions cataplexy is partial and clinical questions as to its presence have to be couched in terms of 'feelings of weakness'. This approach is more likely to alert the narcoleptic to mild symptoms such as/

/as weakness of facial muscles or of a hand on emotional occasions and very frequently the patient will describe that he avoids such situations. The most frequent example is the narcoleptic who avoids laughing heartily but several patients also mentioned how they tried to avoid emotional scenes at home. It was several times put to me in discussing symptoms that the narcoleptic 'was alright if I can take things easily'. In practical terms it is clear that estimates of the age of origin of the disorder must be treated with caution and the possibility that the disorder has been present for some time, possibly all the life of the individual, cannot be ruled out. Narcolepsy has certainly been recorded in children (YOSS and DALY, 1960).

It may be fair to accept that the age of onset indicates a 'shift' in the intensity of symptoms and that many of the aetiological agents which individuals cite - head injury, influenza or other febrile conditions are either precipitants or events which have drawn attention to the sleep symptoms. In this study the incidence of such 'aetiological' conditions was not impressive and it would seem more reasonable to see them as precipitants.

Accepting these limitations the study did show that in the twenty seven patients in the idiopathic narcoleptic group 85% located there first cataplectic attack to within a period of five years from the first sleep attack and 44% considered the symptoms concident. However this leaves/

/leaves an importantvgroup who consider that cataplexy has post dated the sleep attacks by a considerable length of time. In this study one subject located his cataplexy eighteen years and another thirteen years following the development of sleep attacks. Again it was found in these cases that the location of cataplexy to this time was dependent on a definite incident. M10 for example presented with the complaint that he developed cataplexy recently when angry with his six year old son and intending to smack the child. Interestingly anger itself did not cause him weakness - he was a construction worker who had been involved in fights and arguments before and since this episode of cataplexy without any weakness. Certainly it was possible to make him very angry in the recording situations as he was Irish and felt very strongly over the Irish problems. This happened without trace of weakness but for him it was the situation of anger with a child to whom he was most attached, which evoked cataplexy. Other feelings of weakness did however occur when he laughed but to him these were nothing, particularly in relation to his massive weakness when attempting to smack the child. Cataplexy can therefore be curiously limited and it is impressive that few patients saw cataplexy as a problem in their lives, on the whole most people were more concerned about the sleep attacks which caused embarrassment, created driving difficulties or meant the housewife burning her ironing or the worker sleeping/

/sleeping past his bus stop or station.

But if the patients can develope cataplexy a long time after the origin of the sleep attacks, would they truly have been incapable of cataplexy before, or is the appearance of recognised cataplexy an indication of a shift in the illness? It will only be possible to attempt to answer this question by following up a group of narcoleptics who have never had or rarely suffer from cataplexy and see if the disorder undergoes an exaccerbation or some 'shift' in time.

Asked what they considered to be the state of their disorder (Table 7), almost half the patient group saw themselves as suffering from a chronic, static disorder. Less than 10% saw evidence of improvement and over 20% seemed aware of fluctuations, possibly exaccerbations. Over 20% also felt they were deteriorating. In that a criterion for inclusion in this study was referral to a clinic it may may be assumed that many patients were requiring more help at that time - i.e. they might well be poorly stabilized in rleation to the illness. In this light it is perhaps surprising that only 42% of the whole group saw themselves as fluctuant or deteriorating. ROTH (1957) described that 7.8% of his narcolepsy group suffered from exaccerbations of symptoms, so that the narcoleptics in this study may represent a more disturbed sample. Equally very few patients in SOURS (1963) group thought their condition was deteriorating so that many surveys suggest that narcolepsy is a relative/

/relative static disorder subject to some fluctuation but with little suggestion of a natural remission. In support of this view is the data on the duration of symptoms. This survey showed that 25% of subjects had recorded symptoms for more than 20 years (Fig. III) and one patient's symptoms had been present for over 30 years. Most surveys have noted the chronicity of these complaints.

One point which emerged early on in the investigation was that most narcoleptic subjects described sleep attacks and hypnogogic hallucinations at the start of sleep, much less frequently during the night. Nightmares were however described through the night. This observation was confirmed by ROTH (1969) and by SOURS (1963). Hypnogogic hallucinations were less frequent in this study than in SOURS (1963) study of patients. Dreams at sleep onset were not mentioned by Sours but considered rare by ROTH (1969). In contrast dreams were frequently mentioned to occur at sleep onset by the narcoleptic patients in this study. It may depend in fact on what the patients considers is a dream and what is a hypnogogic hallucination.

Basing many of my questions on the data of SOURS (1963) allowed for greater comparison between the two groups in many areas. I found that the common associated narcoleptic symptoms were vivid dreams (90% level); mild appetite increase (50%); mild obesity (40%) and frequent headaches (43%). Less frequently severe obesity (20%) disturbed sleep (27%), severe psychiatric disturbance (20%) occurred.

Less significantly associated complaints of severe appetite increase (10%), severe anxiety (2%), mild depression (13%), occasional headaches (13%), blackouts (13%), irritability (17%) were noted.

In contrast to Sours, no instances of sleep walking occurred in the group and many of the symptoms noted by him - such as dizziness, various aches and pains, nocturnal enuresis, amnesia, impotence, dysarthria, were scarcely mentioned. It could be said that I obtained more psychiatric data from my patients while he obtained more data on 'physical' disorders. It is not easy to explain this observation. It occurs in the findings of other workers. For example ROTH (1969, 1966) is not convinced that psychiatric disorders occur more frequently than in other populations while RECHTSCHAFFEN and DEMENT, (1963, 1966) were more impressed by the frequency of psychiatric disorders in the patients studied. Certainly all my subjects were seen at a psychiatric unit and knew I was a psychiatrist, but I was not aware that the data they gave me was seriously out of line with what they had given at the initial consultation with another physician and neurologist.

Whatever the reason 77% of this group showed some evidence of psychiatric disorder and 20% of the group had suffered from a psychotic illness. While there was a range of personality problems, I was struck by a constellation of personality traits shown by 23% of the group. They were noteable for their vagueness and almost indifference in the/

/the interview situation. They made little emotional display and were inert, passive and apathetic. Their plans for the future, ambitions and drives were clouded or unreal and they gave the general impression of drifting in an aimless fashion. Many times after the initial interview I made a comment that I felt the patient so uninvolved in the situation that he or she would not return for a sleep recording or may turn up on the wrong night. But in fact co-operation was excellent. In keeping with this impression was the fact that for many patients referral came at a time of a natural lull in their lives. For example, three patients were involved with divorce proceedings, either waiting for a court hearing or some other move in the proceedings. Another female patient (F2) returned to Edinburgh from abroad feeling guilty about an aged relative and having dealt with the situation, seemed unable to decide about herself until she arrived some months later and announced that she was emigrating to Rhodesia. Another female patient (F4) suddenly announced that she could not complete the series of recordings as she had decided to leave for Australia and several other patients were between jobs. It may be that patients were using a natural 'lull' to seek attention for a persistent chronic complaint and this was the explanation for the indecision and apathy in the clinical picture. Alternatively it may be that referral is due to the fact that at a time of 'lull' in their lives, patients were more troubled by their symptoms and more concerned about the disorder.

In order to settle this argument we need more information on the narcoleptic patients in the community who may be 'stabilised' narcoleptics who are not particularly concerned about the disorder. If the sample was large enough and representative of the overall group of narcoleptics many of these observations would possible be minimized. It is interesting that it is ROTH (1957) who has seen the largest number of patients in recent times who insists that psychiatric disorders are not prominent in narcoleptic patients and an attempt by SMITH (1959) to apply psychological tests to a small group of narcoleptics to isolated evidence of psychiatric disturbance was inconclusive.

One necessary enquiry is whether the psychiatric disorder, if it is present, is primary or secondary to the narcoleptic disorder. Much of the published literature on narcolepsy as a psychiatric disorder is based on the view of the function of sleep as a retreat from reality or alternatively as a retreat into fantasy in a wish fulfilment sense. (VOGEL, 1960). This is primary gain but it is not easy to delineate between primary gain and secondary gain. Chronic symptoms are frequently used in order to defend the individual or manipulate the environment and secondary gain/

/gain is a feature of normal living and particularly prominent in all chronic disorders.

In this series of patients it was frequently clear that sleep attacks filled a role in the daily functioning of the individual but this was not their primary function as many patients found that when anxious or active they had less frequent sleep attacks.

Physical investigations were unhelpful.

Thyroid disorders, and hypoglycaemia were not found. Cerebrospinal fluid was normal in all cases and there was no radiological evidence of pituitry disease. Polycythaemia was absent in this group.

In summary, while this group bears many similarities on clinical grounds with the patient group described by SOURS (1963), I am less convinced that there is good evidence for accepting the findings as representative of the disorder of narcolepsy in the general population. In this group there is evidence that patients' testimony about symptoms and their onset is rarely objective and hypotheses built on such data are often misleading. Data regarding the incidence of the disorder would require a comprehensive screening system of patients at the general practitioner's surgery rather than a hunt through the classified files of a neurological clinic, and if for some reason connected with the drugs used to treat narcolepsy, data of this type was needed, approaches should be made to the public direct.

Sleep attacks and cataplexy are the most frequent presenting symptoms and less than one narcoleptic in five admits the full tetrad. Also many narcoleptics have symptoms of general hypersomnia.

Generally narcolepsy is a chronic disorder usually presenting in adolescent life and while subject to some fluctuation, rarely if ever remitting for a period.

In contrast the clinical group of symptomatic narcolepsy is markedly heterogenous. While male cases predominate, sleep attacks and extended sleep are the usual symptoms and cataplexy was admitted by two patients. Definite evidence of cerebral damage was present in all cases and the pathology was usually one that produced patchy cerebral disorder - encephalitis, carbon monoxide poisoning and cerebral metastases. However frontal damage and basal fracture of the skull with some presumed brain stem lesion were also noted. The clinical picture was generally that of a drowsy irritable individual prone to more definite sleep attacks. Headache, anxiety and depression were frequent symptoms and some weight gain occurred. Sleep disturbance at night was less frequent that in the idiopathic narcoleptic group and cataplexy was less common;

Physical investigation did not reveal any thyroid dysfunction or hypoglycaemia and skull X-rays confirmed the lesions in two head injury patients. Raised/

/Raised cerebro spinal protein was found in both patients known to suffer from encephalitis, but no polycythaemia was found.

On clinical grounds, symptomatic narcolepsy is diagnosed obviously when patients complain of sleep attacks with or without cataplexy and there is an adequate history of cerebral injury. It is noteable that no examples of a family history of the disorder occurred in this group, and other narcoleptic symptoms were also absent, i.e. no sleep paralysis or nocturnal hallucinations were found in these patients.

The concept of symptomatic narcolepsy arose as investigators discovered narcolepsy symptoms in post encephalitic patients and in post head injury cases. The literature confirm that if sleep attacks and cataplexy are accepted as evidence of narcolepsy, it is not possible to distinguish on clinical grounds between symptomatic and idiopathic narcolepsy and symptomatic narcolepsy may arise secondarily from a vast array of pathological disorders, particularly those producing multiple small lesions of the cerebral axis or frontal lobes.

On clinical grounds it was difficult not to see the patients in this group as narcoleptic although as a group they presented in a more apathetic, disinterested drowsy fashion and in particular it was difficult to form any definite relationship with these patients. Getting them to the laboratory was very difficult and I never did succeed in recording diurnal sleep in M4. It is difficult/

/difficult to find a group of symptomatic narcoleptics in the current literature with which to compare this small group. SOURS (1963) had obvious difficulty in obtaining up to date information on his ten post encephalitic patients. He notes that they had originally complained of sleep attacks and cataplexy, but also that their somnolence was frequently paroxysmal and of longer duration than that of idiopathic narcolepsy. Clinically these patients were recorded to be slow and impoverished, presented appetite and polydipsia as well as evidence of neurological deficits. Many had sleep reversal problems and were irritable and labile in affect.

The 'organic' associated symptoms were also present in ROTH (1957) cases.

This study does confirm the persistence of the narcoleptic symptoms in the post encephalitic patient as in one case ~~of~~ where sleep attacks had been present forty five years.

Idiopathic Hypersomnia

This clinical group is in fact extremely heterogeneous. Basically the diagnosis depends on a complaint of prolonged or extended sleep, but all patients describe how like a narcoleptic they sleep in any situation which condones drowsiness. They differ clinically from the narcoleptic group in many ways. In the first place they do not recognise sleep in the day as an 'attack' which is often the presenting complaint of the narcoleptic. Narcoleptics as a group are very emphatic that many sleep attacks have a characteristic/

/characteristic sudden and irresistible quality which demands sleep. Hypersomniacs in contrast complain of increasing drowsiness leading to sleep. Great efforts directed towards activity can on occasion postpone rarely abort an attack. In contrast the hypersomniac talks more of a heavy, persistent feeling of fatigue and drowsiness, which makes him lethargic and often clumsy. This is more reminiscnent of the concept of 'sleep drunkeness' (ROTH, 1962) seen in the clumsy activity of the somnambulist or in the person roused suddenly from sleep. Sleep drunkeness is prominent in many hpyersomniacs who often return to bed after breakfast or fall asleep again during toilet activities. Their diurnal sleep is longer on average than the narcoleptic and many hypersomniacs claimed that diurnal sleep periods were of approximately an hour's duration. The episodes of prolonged sleep were more variable and it was clear that sleep of over 14 hours was not common. Some subjects were impressed that episodes of prolonged sleep were paroxysmal or related to mild general illness such as colds or influenza. Other patients gave clear illustrations of how prolonged sleep filled spare time at periods in their lives. One subject described how when stuck in camp in his Army days he filled his leisure time entirely with sleep and slept away week-ends.

Cataplexy, feelings of weakness associated with emotion, hypnogogic hallucinations and sleep paralysis were not noted/

/noted in this group and the nocturnal sleep of the group as a whole was untroubled and devoid of any disturbance.

An adequate clinical history including an interview with a relative allowed for more accurate diagnosis of functional hypersomnia in five cases. Three were clearly abusing drugs. Suspicion was aroused in one case (F5) because of a typical grand mal attack which was the actual reason for hospital admission. F5 was extremely variable and her husband gave a clear account of atoxia, slurred speech with increasing drowsiness which fluctuated in the day. F6, a young girl admitted to a psychiatric hospital because of personality problems was found to be excessively sleepy during the stay and at first thought to be withdrawing. Evidence of ataxia was definite but slight and the first confirmation of drug abuse arose from a routine electroencephalographic examination. It is curious that no mention is made in contemporary literature of drug abuse as a case of hypersomnia and as this aetiological factor was present in almost a quarter of the cases in the idiopathic hypersomnia group in this study, it is obviously an agent which must be excluded if idiopathic hypersomnia is to stand as an entity.

Equally, and adequate history enabled the basis of sleep complaints of F2 and F3 to be understood. In fact both these patients were suffering from a degree of sleep deprivation for definite interpersonal reasons within marriage. What was interesting was that both these women presented to their/

/their general practitioners requesting stimulants to deal with their sleep attacks and F2 in fact did receive some medication. Neither patient gave direct information about her nocturnal sleep and it was only when the husband of F3 was interviewed, that her customary sleeping habits were revealed. F2 however described her short night sleep in quite an unconcerned way apparently unable to see the connection of these short nights with her sleep attacks.

Removing these cases leaves a group of eight patients with a strong male preponderance (6M, 2F). It is of interest that TAKAHASHI (1964) also showed a 3:1 preponderance in this group of 28 hypersomniacs. While the age range of this group is wide (6-59), more than half the cases are in the 20-29 range and in fact the commonest case is that of a young male, aged 20-21. All subjects in this group considered the disorder to date to adolescence, but like the narcoleptic group further contact with the individual patient over the period of sleep studies made it likely that some sleep disturbance antedated adolescence. Complaint of hypersomnia was usually related more to a specific instance during adolescence or to a more general awareness of self at this period in their lives.

Obesity, appetite increase and headaches were the most frequent associated symptoms while anxiety in a non specific way was frequently present. Medical investigations were unhelpful. No evidence of thyroid dysfunction or/

/or hypoglycaemia was found.

Skull X-rays, cerebrospinal fluid and haematological investigations were also unhelpful. All the patients in this group were clinically of normal intelligence, and two were in fact university students. No relevant family history were obtained from many patients although in four instances there was evidence of prolonged sleep or sleep attacks in a first degree relative.

It is interesting to compare this group with that of TAKAHASHI (1965). He noted a male preponderance and found hypersomnia was commonest in early adult life, most cases resulting spontaneously after the age of thirty years. Somnolent episodes, and these cases were erratically spaced and related to trivial illnesses or 'physical or mental' exhaustion. During somnolent episodes, he recorded that his subjects were rousable but remained drowsy and relatively inaccessible. Physical investigations were largely unhelpful although some dilation of the ventricular system was noted in several cases.

In keeping with the persistent drowsiness of the hypersomnia period, TAKAHASHI found lowered blood pressure, pulse rate, excretion of urine and basal metabolic rate. Unfortunately TAKAHASHI gives little information on the psychiatric background of his cases.

In my assessment I was struck by a characteristic constellation of symptoms and personality traits in this group.

This 'syndrome' was characterized by apathy and uninvolvement at interview with conspicuous lack of drive and a general 'loss of volition.' There was marked over dependancy on parental figures and in response to some environmental threat, the individual classically retreated, giving up job or course and returning home to retire to bed and sleep. The dependancy was frequently associated with hostility towards parents and this was resolved by retreat into sleep. The situation of the 'sick child' but protected from the hostile feeling by sleep, was frequently described by the patient. Involvement in activity outside the home classically reversed the hypersomnia. So one student described how difficult it was to get to disagreeable lectures and tutorials but in his third year he was involved in a 'project' which on occasion demanded that he got to the laboratory at frequent intervals occasionally in the middle of the night. He had no difficulty with this task.

A syndrome of 'uninvolvement' continually recurs in the whole group of narcolepsy and hypersomnia disorders but nowhere is it as well marked as in these young adult male hypersomniacs.

In this respect, the patients in this group resemble those described by PAI (1950) and GOLDSTEIN (1958). It is a phenomenon of the literature that more attention has been given to cases of periodic hypersomnia with some disturbance of eating (the Kleine Levin Syndrome) than to psychologenic/

/psychologenic hypersomnia. PAI (1950) clearly saw that from his studies psychological disturbances were the prime factor in hypersomnia generally. But this is too limited a view as many of the papers on cases labelled Kleine Levin syndrome describe a very 'organic' picture with confusion and disinhibition as well developed symptoms.

It would seem logical to see idiopathic hypersomnia as a bipolar syndrome with cases of clearly psychogenic hypersomnia at one extreme and cases in which there is definite evidence of frontal lobe/diencephalon dysfunction at the other.

The understanding of the individual case then requires that any evidence of a midbrain disorder must be eliminated by neurological investigation, then psychiatric and social investigations should always follow. The literature suggests most strongly that in the past it has been customary for each discipline to claim the cases and insist that the explanation lies in their speciality, pinning 'organic' labels on any slight neurological abnormality and 'psychogenic' labels on any dynamic explanation.

Nevertheless in this series, psychological hypersomnia alone is present. Whether it is a sampling problem in that I function as a psychiatrist rather than a neurologist, or is a ~~tone~~ true reflection of the state of the disorder in the community is a point of argument. Publicity did in fact present me with several cases of hypersomnia but in none of these was there evidence of a distinct organic basis for the/

/the syndrome.

Finally I was struck by the fact that the preponderance of young adults in this syndrome, may be explained by the fact that sleep 'matures' or 'disintegrates' with the passage of years. Young people get to sleep easily and their sleep is more continuous than that of the middle aged and elderly. Under stress it is therefore easier for the young to retreat into sleep as a defense, than it is for the older subject. This might explain why Takahashi found that hypersomnia tended to remit spontaneously with age and few cases continued to have symptoms past the age of thirty years.

It may be that 'drowsiness' which may represent some incapacity for arousal to inhibit slow wave sleep, is in fact distributed overall in a Gausian distribution and that subjects who develope hypersomnia are in fact individuals from the lower end of the distribution curve - i.e. those who are readily and frequently drowsy. It is obviously difficult to collect a representative sample of hypersomniacs but studies of vigilance in such individuals may in fact enable this hypothesis to be adequately tested.

The Kleine Levin Syndrome

Three cases were referred during this period who complained of hypersomnia in the form of prolonged sleep and of eating problems. Despite the small number of this subgroup there are similarities with the larger idiopathic hypersomnia group. The preponderance is towards the young/

/young adult male, as the sex ratio is again 2:1. Subjects were able to localise a period of 3-4 days sleep in their early adolescnace as the starting point of the disorder usually in relation to a mild physical illness or some point of personal crisis. However these subjects were frequently able to oversleep and complained of irregular drowsiness. The overeating symptom was more variable. While it did appear to coincide in time with the sleep disturbance, both male subjects, who were in fact moderately obese, saw the symptoms as an increase in appetite without any definite craving for a particular food. The female patient in contrast was not prepared to view her overeating as an appetite increase but insisted that there were times which she had an unsatiable desire for sweet things; she would buy large quantities of cakes and sweets which she gorged until she was actually sick. Her account was of interest in that she insisted that the 'craving' was present even though she already felt nauseated, and this disorder of eating frequently occurred independantly from her periods of oversleep. She was in fact of normal weight. The commonest associated symptoms for these patients were anxiety and depression, with headache and some irritability. Nocturnal sleep was uneventful.

In this group there was little evidence of any definite familial factors, and investigations did not show evidence of thyroid dysfunction or of any neurological disorder.

Polycythaemia was absent.

I saw one male patient during a period of hypersomnia. He was definitely rousable but left to his own devices, returned to sleep. Orientation was normal and responses to questions were also carried out in a disinterested but accurate way. The overall impression was of a drowsy disinterested man, who was resentful of questions. Recent memory tests were also normal.

Psychiatric assessment of these subjects was in fact relevant. Periods of prolonged sleep were frequently seen to be precipitated by a rise in tension in the family or school environment and the original 'illness' was seen to serve a definite purpose in allowing the individual to retreat to a more dependant situation often effectively altering the attitude of the family in the process.

For example, the female patient developed an episode of prolonged sleep after admission to the school sanitorium for an 'influenza type illness'. In her family, affection was rare and great emphasis was put on academic performance. An older brother had opted out of this arrangement and left school to work in an office, so the focus of the family aspirations fell on the patient. At first she was pleased to succeed but a growing resentment increased her ambivalence. The influenzal episode occurred two months before important examinations and as a result of her oversleep she was taken home and on an extensive convalescent holiday - the whole episode being interpreted by the school authorities as/

/as related to excessive study. She still recounts how the parents were able to give her considerable affection and support when she was ill.

But while some episodes are clearly understandable in the light of personal dynamics, this is not always the case.

These subjects frequently saw the hypersomnia episode connected to a feeling of angry hopelessness which was very reminiscent of a depressive disturbance.

The overeating symptom is difficult to understand. In these patients there was no hint of any psychotic disinhibition of behaviour leading to loss of control of eating. The male patients in fact felt hungry and it was the female patient who presented more definite gorging.

The picture is reminiscent of the unusual female depressive, who when disturbed, overeats certainly to the extent of reversing the normal weight loss in depressive illness, and occasionally overeating to the point of vomiting. Overeating as a symptom of personal distress is also quite common in adolescents and young adults and this is also the age group in which can sleep excessively. It is possible to understand these cases as an exaggeration of the over sleeping, overeating symptoms of the disturbed adolescent.

If then we label these cases as psychogenic Kleine Levin syndrome do they differ significantly from the patients in the idiopathic hypersomnia group? Apart from the fact that there is an appetite disorder symptom present, they do not differ/

/differ in any way.

But these cases do not conform to the Kleine Levin syndrome defined by Critchley. Although he saw the disorder as limited to young adult males, his cases were noteable for their organic confusion or psychotic manifestations. The description of cases by GARLAND (1965) and ROBINSON (1951) also point graphically the frontal lobe syndrome aspects of the disinhibition and euphoria seen in these cases. Cases described by CRITCHLEY (1952) showed definite schizophreniform psychotic symptoms as well as organic confusional symptoms.

One striking difficulty in discussing these 'organic' syndromes is the fact that there is a lack of evidence that the patients sleep. Sleep in these cases is an appropriate term only by virtue of the fact that patients are inert but rousable and the inactive period does not lead to incontinence. However, as OSWALD (1969) pointed out there was a distinct lack of EEG or physiological monitoring of these patients which would allow a definite diagnosis of sleep. Sleep changes in the EEG of a patient are mentioned by GILBERT (1964) but more recent studies have not confirmed this finding. The female patient described by DUFFY (1968) was so unco-operative during the hypersomnia period that it was impossible to record an EEG. In one case described by BONKALO (1968) high voltage slow waves were recorded from frontal and temporal zones during an episode of hypersomnia, THACORE (1969) also records generalized data and theta activity in the EEG of a boy of/

/of thirteen years during a 'hypersomnia' episode. Sleep spindles were not seen. Similar findings in a study of another thirteen year old boy with a Kleine Levin syndrome described by ELIAN (1969) emphasize the paroxysmal qualities of the EEG and the authors correlate these findings with the observation of TAKAHASHI (1965) that the convulsive threshold to metrazole is decreased in hypersomnia patients. Finally GREEN (1970) described a case of Kleine Levin Syndrome in which the EEG during the 'hypersomnia' episode was paroxysmal and contained diffuse slow activity. No sleep spindles were present although in a 'normal' period, a sleep recording was obtained from this nineteen year old male subject which was quite normal.

This recent literature supports the concept ~~that~~ of a paroxysmal disorder of brain function possibly centred on the diencephalon, which promotes the development of episodes of confused, disinhibited behaviour associated with withdrawal and alteration or clouding of consciousness.

The Kleine Levin syndrome as outlined by Critchely would be compatible with this description and it should not be assumed to be a form of hypersomnia without good physiological evidence of sleep. It is also true that there are fluctuant and recurring psychotic disorders often resembling schizophrenia in their symptomatology CRAMMER (1959) described some states under the term of schizoaffective and LEONHARD (1961) described what he termed the cycloid psychoses.

If the original case such psychoses were associated with disturbance of eating, then they too might be included in the Kleine Levin syndrome.

It is obvious that the term Kleine Levin syndrome has the disadvantage that it may be interpreted in many ways. To include within its definition psychogenic hypersomnia of the type described in this study would be confusing, as these cases bear more resemblance to the idiopathic hypersomnia group than they do to Critchley's cases.

However to restrict the use of Kleine Levin syndrome to young makes is hardly justified in the light of recent reports although it remains true that young adult males remain the backbone of all series of cases of hypersomnia. Nevertheless female cases strictly compatible with the male subjects exist.

It is imperative that if this syndrome is to be kept in the general group of hypersomnias, unequivocal evidence of sleep must be presented. Episodes of disordered consciousness must be valuated correctly as their implications are different.

Finally again it would seem logical to explore the basis of this syndrome not only from an organic neurological basis but also from a psychiatric viewpoint so that any form of periodic psychosis is correctly identified.

While it has been reported that EEG changes compatible with slow wave sleep has been recorded in patients following cerebral injury (CHATRIAN, 1963) no report of the regular/

/regular alteration of slow wave sleep and REM sleep during states of coma have been made and sleep must be defined in terms of the regular alternation of these two states.

Clinical data

The Pickwickian syndrome

The Pickwickian syndrome as described by BURWELL (1956) and elaborated by the later workers (HACKNEY, 1959, DRACHMAN and GUMMIT, 1962) was an attractive clinical-physiological model which explained most convincingly the drowsiness and hypersomnia symptoms. Obesity, leading to impaired alveolar ventilation and hypersomnia, compensatory secondary polycythaemia were the obligatory components of the disorder. Drowsiness was due to hypersapnia and DRACHMAN and GUMMIT (1962) proposed that the recurring drowsiness cycle of arousal - drowsiness - light sleep - arousal could be understood as an effect of the hypercapina and insensitivity of respiratory chemoreceptors allowing apnoea and anoxia to develop which ultimately led to sudden arousal.

This model was developed principally by respiratory physiologists, but a rather differant approach by sleep researchers led to different conclusions.

JUNG and KUHLO (1965) defined the Pickwickian syndrome in terms of the sleep disturbance, i.e. frequent short episodes of spontaneous sleep with apnoea. Three patients were studied and recorded during overnight sleep - the first investigation of nocturnal sleep.

Initial investigations showed that while these patients were moderately obese, one subject had the typical snoring respiration during sleep which antedated the weight gain by five years.

Polycythaemia was absent in one case, and not gross in either of the other cases. Blood gases in one case were within normal limits. Nevertheless records of diurnal sleep in all three cases showed the arousal - drowsiness - light sleep - snorting arousal. Interesting however, weight loss in each case was associated with both subjective and objective improvement.

Nocturnal sleep followed the pattern of diurnal sleep. Drowsiness was associated with ineffective respirations and apnea lasting 5-15 secs. Stage II slow wave sleep with longer apneic periods (20-40 secs) were associated with cyanosis and bradycardia and myoclonic jerks of the limbs. Abortive respirations culminating in a great snore associated with marked K-complexes and muscle artifact, led to arousal. These shallow cycles of sleep interrupted by periods of arousal made up most of the night's sleep. Very rarely was Stage III slow wave sleep seen in these records and no Stage IV slow wave sleep was seen. REM sleep was also severely depressed and it was noted that surprisingly in REM sleep respiration was regular and not noisy. Jung and Kuhlo found that CO_2 levels were severely raised during the apneic periods and considered that the cause of the apnea was an atonia of the tongue and pharynx which accompanied drowsiness and produced obstruction of the airway. Weight loss was found to alternate the respiration and sleep difficulties.

These authors conceived of the Pickwickian syndrome as an acceleration of the normal relationship between sleep and respiration. Referring to the work of ROBIN (1958) and BULOW (1963) they related the fall in respiratory rate and occasional short apnea with the slight increase in pCO_2 seen in the normal subject at sleep onset to the typical Pickwickian disturbances as merely a quantitative rather than a qualitative change. The critical factor in this change was the atony of the pharyngeal muscles.

These observations were confirmed and extended by GASTAUT (1969). Gastaut objected to the respiratory physiologist's concept of the Pickwickian syndrome on the grounds that hypercapina ought to exert more consistent somnolence, not the intermittent disturbance found in these subjects. One subject was described in detail. Obesity was not associated with polycythaemia or hypercapina in this case, but the diurnal and nocturnal sleep changes were identical with these described by Jung and Kuhlo (1965). However no REM sleep was identified and the maximum time spent in any stage of sleep was less than 30 minutes. Short periods of Stage IV slow wave sleep were seen, however, towards the end of the night. Gastaut considered that the Pickwickian patient was insensitive to CO_2 hyperventilatory stimulus but as pO_2 fell during the period of apnoea it acted directly on brain stem centres and stimulated arousal with restoration/

/restoration.

These authors were very convinced that the apnea was the result of a massive obstruction of the pharynx by the tongue and pharyngeal muscles which they postulated to be caused by hypotonia and massive infiltration of fat into these muscles. The episodes of drowsiness could be understood as arising from some basic disturbance of the sleep regulation brain stem centres, or could possibly be due to the fact that Pickwickian patients were chronically fatigued as a result of the poor night's sleep.

From these observations, ESCANDE (1967) proposed that the Pickwickian syndrome should be subdivided, i.e.

Syndrome Type Burwell. Obesity, polycythaemia and hypercapina as well as the typical interrupted sleep pattern.

Syndrome Type Joe. Obesity and classical sleep disturbance, but no evidence of alveolar hypoventilation.

In a series of papers SCHWARTZ and ESCANDE (1966, 1967a, 1967b) extended these views. Serial radiographs during the respiratory-sleep cycle of one case revealed elevation of the diaphragm with ineffective or absent rib movement followed by jerking respiratory attempts using accessary muscles and spasmodic aropharyngeal contractions leading to successive snorts. They discussed the respiratory obstruction theory and considered that there was evidence to support both apnoea of central origin and obstructive apnoea which led frequently to a mixed type of respiratory ceasation.

Similar clinical sleep disturbances with obesity without hypoventilation have been reported by TAKAHASHI (1967) and KUHLO (1968).

The Pickwickian subjects in this study fulfil the obesity, sleep disturbance criteria of DRACHMAN and GUMMIT (1963). They lack the hypercampina at rest, and polycythaemia which are necessary in the alveolar hyperventilation Pickwickian model (Type Burwell).

Therefore they may be included with the cases of JUNG (1965) and GASTAUT (1966). However in these subjects there is no evidence of any major airway obstruction which has been postulated by so many investigators (CATON, 1880, KRABBE, 1942, JUNG, 1965, GASTAUT, 1966).

It would seem more reasonable to postulate that the Pickwickian patient shows an abnormality in the regulation of respiration in relation to sleep (KUHLO, 1968). The process of sleeping is associated with hypoventilation, short periods of apneoa and mild hypercapina (INGVAR and BULOW, 1963, DURON, 1966). This has been unanimously interpreted as the effect of a decrease in the excitability of the respiratory centre (BIRCHFIELD, 1959, SNYDER, 1964). Accepting this effect, it must follow that any reduction in the activity of the central centre for respiration must allow only moderate changes in blood gases to occur, or sleep will be threatened. Pickwickian patients in this sense present a gross exxaggeration of the normal physiology. They seem unable most of the time to continue normal ventilation when slow activity occurs/

/occurs in the EEG. Anoxia presents a severe ventilatory stimulus and this generally results in arousal with snorting respiration. These Pickwickian cycles of sleep severely disrupt the cycles of slow wave sleep and depress REM sleep.

Subject M1 demonstrated that the insensitivity of the system allowed anoxia and hypercapnia to build up during the night - and that respiration was effectively 'decoupled' from sleep during a REM period in which pO_2 was severely depressed.

However Subject M2 failed to confirm this overall insensitivity to pO_2 and pCO_2. He succeeded in preventing pO_2 levels from dipping beyond what can be accepted as normal but dips of a minor character occur. It was however noticeable that he kept the typical pickwickian respiratory snorts going during most REM sleep periods and rather unfortunately, while occasional cycles of slow wave sleep occurred, on the night when arterial catheter samples were taken he never fell below Stage II sleep. It is not ethical to expose patients to repeated arterial catheterization so at the moment I am unsure whether M2 would allow his nocturnal pO_2 to fall further in a cycle of slow wave sleep.

These studies however give little data to conflict with GASTAUT's (1966) hypothesis that a fall in pO_2 is the arousal stimulus to break up the apnea/ineffective respiration and dissrupt sleep in the Pickwickian patient. However both these subjects when <u>awake</u> show evidence of a <u>normal</u> hypoxic drive. So it is clear that sleep effectively creates a/

/a difference either in the sensitivity of the central respiratory centre or in the peripheral chemoreceptors. GUAZZI and FREIS (1969) showed that the differentiation of sinoaortic receptors in the cat, the rise in pCO_2 and fall in pH and pO_2 with sleep onset was more marked and the levels of blood gases during sleep were more erratic. From their results, they argued that the aortic chemoreceptors formed a buffering system in sleep which damped fluctuations in the blood gases, but the hypoventilation of sleep was in fact a central mechanism.

While it is acceptable to postulate that the Pickwickian syndrome is bipolar with the possibility that cases exist between the respiratory Pickwickian group and the non respiratory group, the rejection of the idea that hpyercapina is responsible for somnolence leaves a problem. Why are 'Type Joe' Pickwickians subject to sleep attacks? GASTAUT (1966) offers the simple explanation that they are sleep deprived by this extremely disorganized night sleep. However this is not entirely acceptable on two accounts.

1. In some studies Dr. D.C. Flenley and I investigated severe bronchitis i.e. patients who had suffered several episodes of respiratory failure. Such patients often press for continuous oxygen administration at night. They will not allow anoxia to increase and further fall in pO_2 continues to exert a tremendous respiratory and arousal stimulus. Their sleep was disturbed by frequent arousals and total/

/total sleep time and REM sleep time were severely curtailed. Occasional REM sleep free nights were found. Yet none of these subjects suffer from sleep attacks or somnolence despite chronic hypercapina. It is however true that SCHWARTZ (1967a) reported Pickwickian sleep cycles in a thin patient with emphysema, but this has not been my experience yet. 2. Sleep deprivation volunteers certainly show a demand for sleep which certainly varies from one time of day to another, and lead to microsleeps but not the sleep attacks of the Pickwickian.

SCHWARTZ (1967) from her experience with patients following neurosurgery, suggests that these diurnal sleep attacks are of 'Intermediate sleep' by which she means a mixture of slow wave sleep and REM sleep which is usual in the first REM sleep period in the night and occurs in the sleep of some normal individuals particularly when on drugs such as hypnotics. However diurnal sleep studies with these patients revealed no traces of REM sleep. Most studies have agreed that REM sleep is less frequent in these patients and one might argue that they are REM sleep deprived, but SOREM periods do not occur in the day and they certainly lack the cataplexy symptoms of the narcoleptic patients.

If it is accepted that the Pickwickian shows a disorder of the central control of respiration, it is reasonable to suggest that he suffers from a similar brain stem dysfunction of sleep control. Neurophysiological data supports the concept of a centre at the lower end of the reticular/

reticular formation as a whole - of which the respiratory centre is a part. This hypothesis is not easy to test in a clinical setting unfortunately and one objection is the presence of obesity as part of the syndrome. This symptome usually is taken to indicate hypothalamic-pituitary disorder. However the recent discovery that growth hormone is actively secreted in sleep (~~HAIDA~~ HONDA, 1969) and appears to be associated with Stage III + IV slow wave sleep (Sassin, 1969) offers the alternative hypothesis that there is a connection between the obesity of the Pickwickian and the sleep disturbance. The clinical observation of most workers that Pickwickian patients improve after weight reduction requires more objective study. I will continue to study both these patients at intervals as a programme of weight reduction with fenfluramine (Ponderax) is conducted. This drug in chronic use increases slow wave sleep and as I have obtained base time growth hormone values in M2 it will be possible to investigate changes in this hormone in relation to clinical improvement.

<u>What is Hypersomnia</u>?

Working within a medical framework, I have not found hypersomnia to be a frequent problem. Fifty-four cases in a five year period suggests that the incidence of hypersomnia is small, and yet many colleagues are surprised that I have personally investigated as many as thirty idiopathic narcoleptics. The literature over the past five years/

/years shows that many authorities, in Japan, U.S.A. and Czechoslovakia have investigated larger groups but these have usually been obtained from known cases on the files of neurological clinics or have been gathered through advertisements.

Discussion with individual patients frequently reveals that symptoms have been noted for years before the point of referral to a physician, so it seems reasonable to consider that hypersomnia is a disorder which can be tolerated very well within the community. Patients present with symptoms of hypersomnia when some other factor of life makes them more aware of the problem, or when associated symptoms show some evidence of change. Excessive sleep is not illness until some change in the patient's situation identifies the sleep or the associated symptoms as abnormal. It follows that if we should require an accurate assessment of the incidence of hypersomnia, only an approach to the individual in the community would allow for reliable figures, but even to do this would require a much more concrete definition of the range of normality for sleep. ~~in relation~~. Such approaches could be accused of 'making' illness so it is customary in medicine to leave the initiation of the referral to the patient or some related agency.

The absence of patients (with the exception of the Pickwickian syndrome) showing evidence of cerebral disease or thyroid disease from this series is interesting.

It may be that such cases are filtered off by the original medical contact and that 'hypersomnia' as a symptom of a wide range of physical diseases is well understood by physicians. In many ways this is unfortunate as there has been very little physiological monitoring of such cases if they are to be included in the general group of hypersomnia it should be established that they show some disorder of sleep. A definition of sleep as a state of relative inertia and unresponsiveness, does not distinguish between early coma states of lowered vigilance and sleep. The physiological definition of sleep as a series of slow wave sleep cycles alternating with periods of REM sleep must be met if these organic disorders can be accepted as examples of hypersomnia. Current sleep research into the sleep of patients with thyroid disease (KALES, 1967) has demonstrated that these disorders do have effects principally on slow wave sleep, but there is no evidence of disturbance of REM sleep or of excessive sleep. Physiological monitoring would allow a distination between a sleep disorder and conditions which provide a disturbance of consciousness or early coma. This argument is also relevant to the distinction between hypersomnia with disturbance of appetite and cerebral dysfunction and appetite disturbance. Recent evidence (THACORE, 1969, GREEN, 1970) strongly supports the contention that at least some of the group of the Kleine Levin syndrome described by CRITCHLEY (1962) should be considered as examples of dysfunction of deep midline /

/midline structures sometimes with alteration of sonsciousness rather than a syndrome of hypersomnia.

If by continuous physiological monitoring it is possible to limit hypersomnia to these people who show evidence of disorders of sleep cycles and REM sleep, this study demonstrates that it is possible to carry out further segregation on aetiological lines. First the patients with the Pickwickian syndrome, whether the explanation of this syndrome lies in alveolar hypoventilation, obstruction of respiratory or some brain stem disturbance, present a distinct disturbance of sleep cycles and REM sleep which seems so consistent that it may be the principalfeature in the Pickwickian syndrome as it is more constant than obesity.

Cases of pseudo hypersomnia occur in this study in the form of abuses or hypnotic or tranquillizer drugs, and individuals who have voluntarily restricted nocturnal sleep for personal reasons and now present symptoms of diurnal sleep as a disorder.

The remaining subjects show a syndrome of the hypersomnia. Sleep studies divide them into two groups:-

1) Those showing evidence of sleep onset REM sleep and its clinical sequences of cataplexy, sleep paralysis, hypnogogic hallucinations and vivid dreams.
2) Those who do not show SOREM sleep.

The process of these two groups is not easy in that identification of SOREM periods requires repeated monitoring/

/monitoring of both diurnal and nocturnal sleep. However the sensitivity of the patient to a loading disc (5G) of laevo tryptophan is an useful accessory test.

It seems desirable to follow historical precedence and reserve the term Idiopathic narcolepsy for this first group, acknowledging that as well as presribing with the symptoms of attacks of REM sleep, such patients also show excessive slow wave sleep.

The second group would be best termed non specific hypersomnias. Some show appetite or eating disorders, others have a disorder of consistent oversleep, while others show phases of oversleep alternating with symptom free periods.

This division is further complicated by patients who complain of sleep attacks but no cataplexy and no SOREM periods. At the time of investigation they do not show any difference from cases of non specific hypersomnia, but it may be that they do developd SOREM periods and cataplexy at some later point in time. ROTH (1969) has proposed the term 'independant narcolepsy' for this type of patient, but in practical terms I do not see that we have enough evidence to segregate these patients on the basis of a prognostic possibility. No-one has has yet had sufficient opportunity to follow up this type of case and test the hypothesis that they are essentially (larval' narcoleptics. No doubt this aspect of the study will be clarified with time.

The clinical group of symptomatic narcolepsy was also found in this study to be divided by the appearance of SOREM periods and cataplexy. Patients with small discrete brain stem lesions, most frequently encephalitic lesions may present SOREM periods. ROTH (1970) in a personal communication also finds this differance and SOREM periods were recorded in less than 40% of a group of fifty-one symptomatic narcoleptic patients and was associated with one incidence of cataplexy in this group.

The distinction between idiopathic narcolepsy and non specific hypersomnia does offer several advantages. In the first place it offers a physiological explanation of the associated narcoleptic symptoms, cataplexy, sleep paralysis and hypnogogic hallucinations as well as providing a basis for the development of a paranoid hallucinatory psychotic illness in some cases, independant of the psychotic inducing properties of the sympathetico mimetic drug.

Secondly it emphasizes that further approaches to the investigation of idiopathic narcolepsy will entail an analysis of the systems underlying and controlling the REM sleep state and also the systems controlling slow wave sleep. While in the non specific hypersomnia patients the disorder is one of the control of slow wave sleep, or alternatively a disorder of sustained arousal.

This study has demonstrated that in idiopathic narcolepsy the disorder is not due to an increased demand overall for/

/for REM sleep, but due to some precocious triggering of this type of sleep so it can occur immediately following arousal and can intrude into arousal. In the narcoleptic arousal fails to completely inhibit the triggering of REM sleep which is the normal. This trigger is so sensitive that it can be actuated by certain and sometimes highly specific emotional experiences and possibly also by dietary factors as the tryptophan load test illustrates.

The physiological strata involved in REM sleep is fairly reasonably understood and it is generally accepted that brain stem, mid pontine centres are the trigger zones which initiate activity in geniculate occipital pathways and in the limbic system as well as caudally via the extra pyramidal system. Evidence is strong that biogenic amines are closely involved in the operation of this system (JOUVET, 1969, DEMENT, 1969). However no entirely satisfactory system of the role of noradrenaline and serotonin (5HT) has been evolved. Jouvet envisaged originally that noradrenaline was the important amine in the REM sleep system at least in the cat but more recently grave doubts that this is equally true of human sleep has arisen (JOUVET, 1969). Certainly the experiments with narcoleptic patients do not supporttthis view. Sympathetico mimetic drugs will not only depress REM sleep but also disrupt slow wave sleep, although it is possible to arrange the dose so that the main effect is an REM sleep. However oral tryptophan has been shown to increase brain serotonin/

/serotonin (HESS, 1961), ASHCROFT, 1965) and significantly increased the duration and intensity of the SOREM sleep period.

DEMENT (1969) has demonstrated that serotonin is significantly involved in the control of REM sleep and in the cat and rat, serious depletion of brain stem serotonin is associated with the development of insomnia and the spread of activity associated with REM sleep - the PGO spikes into arousal. This can be corrected by injections of 5-hydroxy-tryptophan.

However we have not yet a satisfactory understanding of the neurochemical factors involved in triggering REM sleep although the difficulties of the narcoleptic certainly promotes this research.

But it is important that the fact that slow wave sleep is also disturbed in narcolepsy is remembered. In practical terms, no treatment aimed to control narcolepsy can be successful unless it also promotes arousal and depresses slow wave sleep. There are now many drugs which depress REM sleep - hypnotics (EVANS, 1968, 1970, KALES, 1969) which however as they promote slow wave sleep, aggravate the narcoleptics sleep attacks involving slow wave sleep; imipramine (HISHIKAWA, 1968) which has little depressing effect on slow wave sleep, and mono-amine oxidase inhibitors (AKINDELE, 1970) which also promote slow wave sleep. In our list of available drugs it is still necessary to include amphetamine and methylphenidate as sympathetico mimetic drugs/

/drugs will also depress slow wave sleep. As far as the narcoleptic is concerned it is important to stimulate the search for a drug which depressed REM sleep, promotes arousal and antagonizes slow wave sleep which is not easily tolerated and does not produce other addiction problems.

Non specific hypersomnia may be dividible into several overlapping groups of patients. There is agreement that the syndrome commonly involves young adult males who show a constellation of psychiatric disturbances hinging on a loss of volition and motivation. Some cases show appetite disturbance but are otherwise no differant from the broad group of young subjects. This subgroup is best understood on a psychiatric basis, and although RECHTSCHAFFEN (1969) has noted a raised pulse rate during sleep in his hypersomnia patients, this was not found by TAKAHASHI (1965) and I have not confirmed it in the two hypersomniac patients I have investigated since I heard of this discovery.

Another subgroup are the patients who complain principally of sleep attacks rather than extended sleep and represent ROTH (1969)'s independant narcoleptics.

Finally a few middle aged subjects who have always been able to sleep for long periods in their lives, develop extended sleep on a more consistent basis, possibly as a depressive symptom.

Undoubtedly the emphasis in this group of non specific hypersomnia patients has been on psychological causes for/

/for excessive sleep. These cases are compatible with hypersomniacs described by PAI (1950), GOLDSTEIN (1958), TAKAHASHI (1965). The number of patients in my hypersomnia group is small and generalizations are difficult. However there are a number of further lines of investigation with these patients:-

1) More systematic psychological testing would put the psychiatric observations on a measurable basis and test these conclusions.

2) It would be extremely interesting to incorporate vigilance testing in this group and test the hypothesis that these are essentially drowsy individuals who can sleep readily at any time.

3) Measurement of circadian fluctuations in this group of patients, i.e. corticosteroid output, body temperature, pulse rate, respiratory and simple performance measures; would test the possibility that these are individuals whose circadian cycles are distorted so that they cannot congregate the low points in each cycle into the sight period, and take longer to readh efficient functioning in the morning.

4) Recent research has shown that slow wave sleep is associated with secretion of growth hormone, which supports the view that sleep is a time of readjustment of metabolism. The frequent association of obesity with/

/with or without appetite change with hypersomnia would suggest that these mechanisms are also disturbed in hypersomniacs.

I hope I shall have a further opportunity to investigate these possibilities in hypersomniac patients.

"No small art is it to sleep;
it is necessary for that purpose
to keep awake all day".

Neitzsche, Human, all too Human.

APPENDIX I.

Clinical studies.

Notes on abreviations.

i. Marital state M. married D. divorced S. single

ii. Family History F. father M. mother Sis. sister

SA sleep attacks P.S. prolonged sleep C. cataplexy

E.S. extended sleep.

iii. Other drugs Pb. Phenobarbitone

iv. Head injury
obesity
appetite
anxiety
depression

Graded 1 mild
2 moderate
3 severe

APPENDIX I.

TABLE I (a)

IDIOPATHIC NARCOLEPTIC (FEMALE SUBJECTS)

SUBJECT	Marital State	Age	CATAPLEXY: Drowsiness	CATAPLEXY: Sleep Attacks (Duration, mins)	CATAPLEXY: Cataplexy	CATAPLEXY: Partial/Total	CATAPLEXY: Hypnogogic Hallucinations	CATAPLEXY: Sleep Paralysis	CATAPLEXY: Prolonged Sleep	CATAPLEXY: Extended Sleep	PREVIOUS HEALTH: Family History	PREVIOUS HEALTH: Head Injury	PREVIOUS HEALTH: Meningitis	PREVIOUS HEALTH: Encephalitis	PREVIOUS HEALTH: Veneareal Disease	Age at first symptom	Relation of Cataplexy to S.A.	TREATMENT: Amphetamine	TREATMENT: Methyl Phenidate	TREATMENT: Other Drug
F1	D	35	+	+ 15/30	+	+ occ	+	+	o	o	sister p.s.	o	o	o	o	16	+2	+	o	Thyroid
F2	S	24	±	+ 20/30	+	+occ	occ	+	o	o	o	o	o	o	o	16	o	+	o	o
F3	D	42	+	+ 10/15	+	+ -	o	o	o	o	F. p.s.	o	o	? flu.	o	18	+4	o	o	o
F4	M	36	±	+ 10/20	+	+ -	o	o	o	o	o	o	o	o	o	18	+1	o	o	o
F5	S	27	+	+ 15	+	+ -	o	o	o	+	o	o	o	o	o	16	o	o	+	Pb occas
F6	M	26	o	+ 10	+	+ -	o	occ	o	o	o	o	o	o	o	20	+4	o	o	o
F7	S	37	+	+ 10/20	+	+ -	o	o	+	+	M. S.A.	1	o	o	o	20	+2	o	o	Pb
F8	S	22	+	+ 20/30	+	+occ	+	+	+	+	o	o	o	o	o	16	o	+	+	o
F9	M	32	+	+ 5/10	?	- -	o	+	o	o	o	o	o	o	o	14	-	o	o	o
F10	M	38	+	+ 20/30	+	+ +	o	+	o	o	F. S.A.	o	o	o	o	16	+4	+	+	o
F11	S	20	+	+ 20/40	+	+ -	o	+	o	+	M. p.s.	o	o	o	o	16	+1	o	o	o
F12	M	24	o	+ 10/15	+	+ -	o	o	o	o	o	o	o	o	o	18	0	+	o	o
F13	S	40	+	+ 15	+	+ -	o	+	o	o	o	o	o	o	o	25	+13	+	o	Pb nocte
F14	M	50	+	+ 10/15	+	+ -	o	o	o	o	o	o	o	?	o	20	+5	o	o	o

TABLE I(b)

FEMALE NATOLEPTIC GROUP n = 14.

CLINICAL INFORMATION.

SUBJECT	Obesity	Appetite Increase	Anxiety	Depression	Headaches	Blackouts	Vivid Dreams	Insomnia	Irritability	Psychiatric Illness	Glucose Level at Duirnal Sleep ug/100 ml	P.B.I. ug/100 ml	Skull Xray	Lumbar Puncture	Haemoglobin G/100 ml	Psychiatric State
F1	2	1	1	o	o	o	+	+	o	o	88	5.2	N	N	14.6	Vague. Drifting
F2	2	1	1	o	+	o	+	+	o	o	86	5.0	N	N	13.6	Vague. Drifting
F3	3	2	o	o	o	o	+	o	o	o	74	3.8	N	N	13.1	Normal.
F4	3	2	1	o	+	o	+	o	o	+	74	7.1	N	N	13.8	Hysterical tracts
F5	3	1	1	1	o	o	+	+	o	+	90	4.2	N	N	13.8	Paranoid Schizophrenia
F6	2	1	o	o	+	o	+	o	o	o	72	4.7	N	N	12.0	Normal
F7	4	3	1	1	+	+	+	+	o	o	82	5.1	N	N	12.8	L. Temp. focus G.M. epilepsy
F8	3	2	o	o	+	o	+	o	o	o	80	4.6	N	N	13.1	Vague. Unsettled
F9	3	2	o	o	o	o	+	o	o	o	80	7.1	N	N	13.6	Normal
F10	4	2	2	o	o	o	+	+	o	o	90	6.2	N	N	12.6	Very tense. Unsettled
F11	2	1	2	o	o	o	+	o	+	+	72	4.7	N	N	12.0	Withdrawn Schizoid
F12	4	3	o	o	o	o	+	o	o	o	70	5.1	N	N	13.2	Hypomanic Personality
F13	3	1	o	o	+	+	+	o	+	o	72	4.6	N	N	14.0	Tense & Anxious
F14	4	3	o	o	+	o	o	o	o	o	88	4.9	N	N	12.8	Normal

APPENDIX I.

TABLE II (a)
MALE NATOLEPTIC
GROUP = n = 16.

			SYMPTOMS								PREVIOUS HEALTH							TREATMENT		
SUBJECT	Age	Drowsy	Sleep Attacks dur. m.	Cataplexy	Partial C. Complete C.	Hypnogogic Hallucinations	Sleep Paralysis	Prolonged Sleep i. e. (days)	Extended Sleep i. e. 8+	Family History	Head Injury	Meningitis	Encephalitis	Veneareal Disease	First Age. Symptom	Relation Cat. to S. A.	Amphetamine	Ritalin	Other (State)
M1	55	+	+ 20/30	+	+ ?	o	occ	o	o	o	o	o	o	+	38	+5	o	o	o
M2	37	+	+ 30	+	+ +	o	+	o	+	o	1	o	o	?	25	o	+	+	o
M3	29	o	+ 10	+	+ +	o	+	+	o	o	1	o	o	+	16	o	+	+	o
M4	22	o	+ 15m.	+	+ ?	occ	occ	o	o	o	o	o	o	o	15	+1	o	o	o
M5	29	o	+ 15m.	+	+ o	o	+	o	o	sis. + S. A. C.	o	o	o	o	16	o	+	o	o
M6	34	o	+ 10m.	+	+ -	o	occ	o	o	o	o	o	? flu.	o	13	+6	+	o	o
M7	39	+	+ 15/20m.	+	+ o	o	o	o	o	o	1	o	o	o	20	+6	+	o	o
M8	59	+	+ 30 m.	+	+ +	+	+	+	+	Sister S. A.	?	o	o	?	18	o	?	o	o
M9	14	+	+ 10m.	?	? -	o	o	o	+	o	o	o	o	o	13	o	o	o	o
M10	34	+	+ 5/10	+	+ +	+	+	o	o	M. S. A.	1	o	o	+	15 severe 31	+18	o	o	o
M11	30	+	+ 30	+	+ -	o	o	o	o	F. S. A.	o	o	o	o	16	+4	+	o	o
M12	49	+	+ 30+	+	+ -	o	o	o	o	o	1	o	o	o	20	o	o	o	o
M13	21	+	+ 15/20	?	o o	o	o	o	+	o	o	o	o	o	15	-	o	o	o

TABLE II (a) Contd.
MALE NATOLEPTIC
GROUP = n = 16.

SUBJECT	SYMPTOMS										PREVIOUS HEALTH							TREATMENT		
	Age	Drowsy	Sleep Attacks dur. m.	Cataplexy	Partial C. Complete C.	Hypnogogic Hallucinations	Sleep Paralysis	Prolonged Sleep i. e. (days)	Extended Sleep i. e. 8+	Family History	Head Injury	Meningitis	Encephalitis	Veneareal Disease	First Age. Symptom	Relation Cat. to S. A.	Amphet.	Ritalin	Other (State)
M14	M/ 26	o	+ 20	ooo	+ -	o	o	o	o	F S.A.	o	o	o	o	18	?	+	o	o
M15	M/42	+	+ 10/15	+	+ -	+	ooo	o	o	o	1	o	o	o	20	o	+	+	o
M16	23	+	+ 20/30	+	+ o	o	o	o	o	o	o	o	o	o	18	o	o	+	o

APPENDIX I.

TABLE II (b)

IDIOPATHIC NARCOLEPSY
MALE GROUP, n = 16.

SUBJECT	Obesity	Appetite Increase	Anxiety	Depression	Headaches	Blackouts	Vivid Dreams	Insomnia	Irritability	Psychiatric Illness	Glucose Level ug/100 ml	P.B.I. ug/100 ml	Skull Xray	Lumbar Puncture	Haemoglobin G/100 ml	Psychiatric State
M1	1	o	1	o	o	+	+	o	+	+	70	4.1	N	N	15.0	Elated paranoid Illness
M2	3	2	1	1	+	?	+	+	+	+	74	5.6	N	N	15.0	Severe paranoid illness
M3	2	2	o	o	+	o	+	o	o	+	66	4.2	N	N	14.6	Explosive and psychopathic
M4	2	1	1	o	+	o	+	o	o	o	61	5.1	N	N	15.0	Anxious, Introspective
M5	3	2	o	o	+	o	+	o	o	o	88	4.8	N	N	14.6	Aggressive Traits
M6	2	1	1	o	o	o	+	+	o	o	84	6.2	N	N	14.4	Normal
M7	2	0	1	0	+	o	+	+	o	o	80	69	N	N	13.8	Aggressive Traits
M8	3	2	o	o	+	o	+	o	+	o	68	5.2	N	N	14.9	Irritable Demanding
M9	3	2	o	o	+	+	+	o	+	o	86	7.2	N	N	14.6	Enuretic. Dull Normal intellect
M10	1	1	o	o	±	o	+	o	±	o	88	5.0	N	N	14.4	Impulsive. Rather aggressive
M11	3	2	1	o	o	o	±	o	o	o	76	7.1	N	N	14.6	Obsessional
M12	3	2	o	o	o	o	+	o	o	o	84	5.2	N	N	14.2	Depressed
M13	4	2	o	o	±	o	o	o	o	o	90	4.3	N	N	14.6	Normal
M14	2	1	o	o	±	o	+	o	o	o	88	4.7	N	N	14.8	Vague. Drifting
M15	4	2	o	o	o	o	+	o	o	o	92	6.1	N	N	14.6	Obsessional
M16	2	2	o	o	+	o	+	o	o	o	90	3.8	N	N	14.8	Ineffectual Drifting.

APPENDIX I.

TABLE III (a)

SYMPTOMATIC NARCOLEPSY n = 6

SUBJECT	Age	Drowsiness	Sleep Attacks Duration (mins)	Cataplexy	Partial Total	Hypnogogic Hallucinations	Sleep Paralysis	Prolonged Sleep	Extended Sleep	Family History	Head Injury	Meningitis	Encephalitis	Veneareal Disease	Age at First Symptom	Relation of Cataplexy to S.A.	Amphetamine	Methyl Phenidate	Other Drug
M1	M/28	+	+ 20/30	o	o	o	o	o	+	o	1 Carbon Monoxide Poisoning.	o	o	o	27	-	o	o	o
M2	M/60	+	+ 20	+	+ -	o	o	+	+	o	o	o	++ at. 15.	o	20	o	+	+	o
M3	M/32	+	+ 30+	o	o	o	o	+	+	o	4 Basal Fracture Unconscious 6 days	o	o	o	26	-	o	o	o
M4	M/16	+	+ 15-20	?	? -	o	o	o	+	o	4 Several Fracture Frontal Lobe damage	o	o Un. 10/7	o	15	-	o	o	Pb 60 mg BD
F1	F/36	+	+ 30+	+	+ -	o	o	o	+	o	o	o	++ at. 27.	o	27	o	o	o	o
F2	F/48	+	+	o	o	o	o	o	o	o	o Mastectomy act. 43. Multiple secondaries Some Cerebral	o	o	o	46	o	o	o	o

APPENDIX I

TABLE III (b)

SYMPTOMATIC NAROLEPSY n = 6

SUBJECT	Obesity	Appetite Increase	Anxiety	Depression	Headaches	Blackouts	Vivid Dreams	Insomnia	Irritability	Psychiatric Illness	Glucose Level at Diurnal Sleep	P.B.I. ug/100 ml	Skull Xray	Lumbar Puncture	Haemoglobin g/100 ml	Psychiatric State
M1	2	1	o	o	+	o	o	o	o	o	92	3.8	N	N	14.6	Moderate intellectual loss. Some euphoria and indifferance
M2	4	3	o	o	+	+	+	+	o	o	71	5.2	N	N	14.4	Mild paralysis agitans
M3	2	1	1	1	+	+	o	+	o	o	80	5.0	N	N	14.8	Apathetic, Depressed Chronic headache
M4	2	1	1	1	+	+	o	+	o	+	76	4.8	N	N	14.4	Marked intellectual loss
F1	3	2	1	1	+	o	o	+	+	o	70	4.2	N	N	13.8	Slow and Pedantic
F2	1	1	o	o	+	o	o	+	o	o	68	5.6	N		13.6	Rather apathetic Confused at times

APPENDIX I.

TABLE IV (a)
HYPERSOMNIA GROUP n = 13

SUBJECT	Marital State	Sex	Age	SYMPTOMS: Drowsiness	Sleep Attacks dur. (mins)	Cataplexy	Partial	Total	Hypnogogic Hallucinations	Sleep Paralysis	Prolonged Sleep	Extended Overnight Sleep	PREVIOUS HEALTH: Family History	Head Injury	Meningitis	Encephalitis	Veneareal Disease	Age at First Symptom	Cataplexy of Sleep	TREATMENT: Amphetamine	Ritalin	Other
F1	S	F	28	+	?	o	o	o	o	o	o	+ 12/14	o	o	o	o	o	18	-	o	o	o
F2	M	F	39	+	+ 20/40	o	o	o	o	o	o	o	o	o	o	o	o	32	-	+	o	o
F3	S	F	52	+	+ 60+	o	o	o	occ	o	+ 48+	+ 14/16	o	o	1	o	o	26	-	o	o	diet
F4	S	F	6	o	+ 60+	o	o	o	o	o	+ 24+	+ 16/18	o	o	o	o	o	4	-	o	o	o
F5	M	F	36	+	+ 60+	o	o		o	o	+ 48-72	+ 14/15	o	o	o	o	o	30	-	o	o	o
F6	S	F	18	+	+ 15/20	o	o	o	occ	o	+ 24+	+ 12	sister p.s.	o	o	o	o	17	-	o	o	o
M1	S	M	59	o	+ 20. 180+	o	o	o	o	o	+ 24+	+ 11/14	o	o	o	?	o	20	-	o	+	o
M2	M	M	42	±	+ 20. 30	o	o	o	o	occ	o 14-16	+ 14/16	F, p.s.	o	o	o	o	18	-	+	o	o
M3	S	M	20	+	+ 30. 40	o	o	o	o	o	+ 48+	+ 16/18	o	o	o	o	o	19	-	o	o	o
M4	M	M	21	+	+ 90+	o	o	o	occ	o	+ 48+	+ 14/16	F. p.s.	1	o	o	o	18	-	+	o	o
M5	S	M	20	+	?	o	o	o	occ	o	+ 48	+ 14/16	F. s.a.	o	o	o	o	18	-	o	o	o

TABLE IV (a) (Cont'd)

HYPERSOMNIA GROUP n = 13

SUBJECT	M6	M7
Marital State	S	S
Sex	M	M
Age	26	20
Drowsiness	+	+
Sleep Attacks dur. (mins)	?	?
Cataplexy	0	0
Partial	0	0
Total	0	0
Hypnogogic Hallucinations	0	0
Sleep Paralysis	occ	occ
Prolonged Sleep	0	+
Extended Overnight Sleep	+ 14/16	+ 12/14
Family History	0	0
Head Injury	0	0
Meningitis	0	0
Encephalitis	0	0
Veneareal Disease	0	0
Age at First Symptom	24	14
Cataplexy of Sleep	-	-
Amphet.	0	0
Ritalin	0	0
Other	0	0

APPENDIX I

TABLE IV (b)

HYPERSOMNIA GROUP n = 13

SUBJECT	Obesity	Increased Appetite	Anxiety	Depression	Headaches	Blackouts	Vivid Dreams	Irritability	Insomnia	Psychiatric Illness	Glucose Level	P.B.I. ug/100 ml	Skull Xray	Lumbar Puncture	Haemoglobin g/100 ml	Psychiatric Illness
F1	2	1	o	o	o	o	o	o	o	+	80	4.7	N	N	12.4	Very over dependant
F2	3	2	1	2	+	o	o	o	o	+	70	5.2	N	N	12.1	Depressed. Marital problems
F3	4	3	0	1	o	o	o	o	o	?	76	5.0	N	N	13.8	Hysterical personality
F4	3	2	o	o	±	o	o	o	o	?	70	6.8	N	N	13.2	Passive dependant Child
F5	2	1	1	1	+	+	o	o	o	+	70	4.8	N	N	12.2	Meprobarmate addict
F6	2	1	1	2	+	+	o	o	o	+	70	6.1	N	N	12.8	Barbituate addict
M1	2	1	0	1	+	o	o	o	+	?	82	3.6	N	N	14.2	Obsessional
M2	4	2	o	o	o	o	o	o	o	?	85	4.2	N	N	14.1	Unhappy married Disatisfied in job
M3	2	1	o	1	o	o	o	o	o	?	83	5.6	N	N	14.8	Unhappy with course at University
M4	3	2	o	o	+	o	o	o	o	?	91	5.2	N	N	13.1	Unsettled. Poor motivation
M5	2	1	1	3	+	+	o	o	o	+	80	5.1	N	N	14.2	Schizoid dependant personality
M6	2	1	1	1	+	o	o	o	o	+	74	5.0	N	N	14.8	Librium overdose
M7	3	2	1	2	+	o	o	o	o	?	70	5.2	N	N	14.2	Apathetic & uninvolved in his course

TABLE V

KLEINE LEVIN SYNDROME n = 3

SUBJECT	Marital State	Age	Drowsiness	Sleep Attacks	Cataplexy	Partial / Total	Hypnogogic Hallucinations	Sleep Paralysis	Prolonged Sleep	Extended Sleep	Family History	Head Injury	Meningitis	Encephalitis	Veneareal Disease	Age at origin of complaint	Cataplexy to S.A.	Amphetamine	Methyl Phenidate	Other Drug
	SYMPTOMS										PREVIOUS HEALTH							TREATMENT		
F1	S	19	o	o	o	o / o	o	o	+	+	o	o	o	o	o	16	-	o	o	o
M1	M	29	+	o	o	o / o	o	o	+	+	o	o	o	o	o	14	-	o	o	o
M2	S	27	+	o	o	o / o	o	o	+	+	F s.a.	o	o	o	o	16	-	o	o	o

SUBJECT	Obesity	Appetite Increase	Anxiety	Depression	Headaches	Blackouts	Vivid Dreams	Irritability	Insomnia	Psychiatric Illness	Glucose level mg/100 ml	P.B.I. mg/100 ml	Skull Xray	Lumber Puncture	Haemoglobin G/100 ml	Psychiatric State
F1	2	4	1	1	o	o	o	o	o	+	75	6.1	N	N	12.8	Immature and labile in affect
M1	3	4	1	o	o	o	o	o	o	?	70	5.8	N	N	14.1	Aggressive and psychopathic
M2	4	4	1	1	+	o	o	o	o	+	76	4.6	N	N	14.6	Inhibertually intellectually inferior, Dependant

APPENDIX I

TABLE VI

PICKWICKIAN SYNDROME

n = 2

SUBJECT	M1	M2
Marital State	M	S
Age	56	36
Drowsiness	+	+
Sleep Attacks dur. (mins)	+ 20	+20
Cataplexy	o	o
Partial	o	o
Complete	o	o
Hypnogogic Hallucinations	o	occ
Sleep Paralysis	o	o
Prolonged Sleep	o	+
Extended Sleep	+	+
Family History	o	sis t.a.
Head Injury	2	o
Meningitis	o	o
Encephalitis	o	o
Veneareal Disease	o	o
Age at First Symptom	46	28
Relation of Cataplexy to S.A.	'	'
Amphetamine	+	o
Methyl Phenidate	o	o
Other Drug	Thyroid	o

SUBJECT	M1	M2
Obesity	4	4
Appetite Increase	3	3
Anxiety	1	o
Depression	o	o
Headaches	+	+
Blackouts	o	o
Vivid Dreams	o	1+
Irritability	o	o
Insomnia	o	o
Psychiatric Illness	o	o
Glucose Level at sleep	75	70
P.B.I. ug/100 ml	4.2	5.1
Skull Xray	N	N
Lumbar Puncture	N	N
Haemoglobin G/100 ml	14.6	15.00
Psychiatric State	Nil of note	Nil of note

APPENDIX II

Notes on abbreviations:-

D(REM)	Delay to sleep onset REM period (mins)
SOREM	Sleep onset REM period (duration in mins)
d	delay to sleep (mins)
D	Delay to next REM period (mins)
TTB	Total time in bed from 'lights out' (mins)
TST	Total time asleep (mins)
A	Time awake (mins)
TA	Number of episodes of arousal over one minute
III + IV%	Amount of Stage III + IV slow wave sleep as a percentage of total sleep
REM %	Amount of REM sleep expressed as a percentage of total sleep
Shifts/hour	Transitions to Stage I (drowsiness)and a arousal per hour of sleep averaged over total night
REM (min)	Number of minutes of REM sleep found in each hour of total sleep
sp	Sleep paralysis episode
Stage I (St. I or I)	duration of stage of sleep prior to onset of REM sleep
Stage II	
Aw	Awake
7.5G	Laevo tryptophan 5G
Des. Deser.	Deseril (methysergide)
Fent.	Fentazin (Perphenazine)
Tof.	Tofranil (Imipramine)

IDIOPATHIC NARCOLEPSY A. FEMALE SUBJECTS

APPENDIX II

TABLE 1

Night	START	D(Rem) (Mins)	SOREM (Mins)	d (Mins)	D (Mins)	TTB (Mins)	TST (Mins)	A	TA (Mins)	III% +	IV%	Rem%	Shifts/ Hour	REM (mins) 1	2	3	4	5	6	7	8	TREAT-MENT
SUBJECT F.I. MARCH - MAY 1965																						
1	22.20	2 Stage I	5	5	75	494	476	1	3	18.6		24.9	6.66	5	20	11	22	14	26	16	8	AM. 10m
2	22.40	4 St. I	7	12	80	--	-	Stopped recording after 90 mins														AM. 10m
3	22.36	6 AW/I	-	6	40	526	490	2	30	20.6		27.1	4.40	20	0	36	18	35	12	6	26	Off 2 day
4	22.42	2. I	2	15	60	-	-	Stopped recording after 90 mins														Off 4
5	22.50	5 AW/I	3	16	70	478	469	2	9	21.5		27.5	4.66	3	36	14	10	29	13	11	16	Off 6
	12.32	3 AW/I	6	AWOKE IMMEDIATELY REM SLEEP CEASED																		Off 8
6	22.40	4 St. I	10	15	72	486	472	4	14	26.4		29.0	4.0	10	21	16	17	28	4	31	10	NIL
7	22.35	2 St. I	25	60	-	-	Stopped recording after 90 mins															T.5G.
8	22.45	4. I	16	24	69	481	462	3	19	26.0		33.1	5.0	16	20	18	22	15	30	18	14	T.5G.
9	22.40	3. I	6	10	74	492	480	2	12	25.8		26.3	4.66	6	32	5	21	11	27	14	10	NIL
10	22.40	2. St. I	39 (nightmare)	-		-	-	Refused to continue to sleep in the laboratory after nightmare														T.5G
11	22.34	3 AW/I	27	35	75	496	490	1	26	25.2		33.5	4.0	27	10	13	29	31	18	32	6	T.5G
12	22.30	1 St. I	13	16	76	510	482	6	28	23.6		27.4	5.66	13	22	16	31	18	14	6	12	Deser. 6m T.5G
13	22.30	10 AW/I	16	30	67	500	491	2	9	22.8		26.7	6.0	16	20	11	41	8	16	0	20	DX6 T.5
14	22.42	6. St.I	12	22	65	489	472	3	17	24.6		31.6	4.66	12	19	24	38	21	10	16	9	DX6 T5G
15	22.36	4 St. I	10	18	84	Stopped recording after 90 mins																DX6 T.5
16	22.40	3 St. I	15	24	106	Stopped recording after 120 mins																DX6 T.5
17	22.41	7 AW/I	11	26	68	486	480	2	6	23.8		32.3	4.0	11	26	22	18	0	36	21	17	DX6 T.5

TABLE 2

Night	Start	D (Rem)	SOREM	d	D	TST	TTB	A	TA	III% +	IV%	Rem%	Shifts/ Hour	REM (Min.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT F.2		JULY - SEPTEMBER 1965																				
1	23.11	6 AW/I	16	25	142	460	449	2	11	23.5		24.1	1.33	16	0	19	0	51	18	18	2	AM. 15mg
2	22.20	4 AW/I	15	26	136	483	479	1	4	24.4		27.8	2.16	15	0	5	21	0	4	4	48	AM. 15mg
3	22.40	3 St.I	14	30	90	459	451	1	8	22.3		28.4	1.83	14	0	2	9	13	44	60	0	AM. 15mg
	12.30	2 St.I	10	22	Woken by Nurse at 12.45 p.m.																	
4	22.40	4 St.I	17	28	92	476	475	1	1	19.1		31.6	3.5	17	12	10	21	1	49	28	12	Off 1 day
5	22.30	5 St.I	30	50	53	472	448	3	24	27.5		38.4	4.0	37	12	19	10	22	33	26	13	Off 3
6	22.45	1 St.I	28(sp)	30	63	478	463	2	15	33.3		37.8	4.5	28	27	10	24	5	19	42	20	Off 5
7	22.40	2 St.I	20	26	73	482	444	4	38	41.4		30.4	3.83	20	10	20	29	21	22	13	0	Off 7
8	22.30	2 St.I	18	30	74	480	463	3	15	17.2		24.0	2.33	18	8	18	11	5	36	15	0	Off 9
9	22.50	4 AW/I	20	28	70	494	487	1	7	22.2		29.4	2.5	20	17	0	10	31	0	54	10	T5G
10	22.30	3 St.I	27	40	62	484	478	1	5	33.8		31.4	2.5	27	17	5	20	27	10	15	29	T5G
11	22.40	2 St.I	30	36	52	474	459	3	15	34.1		30.5	1.83	30	23	11	16	11	7	42	0	T5G
12	22.45	3 AW/I	10	20	188	456	454	1	2	27.2		29.3	2.0	10	0	0	0	23	39	23	38	Deser. 6mg
13	22.40	4 St.I	12	22	53	472	448	3	24	27.5		25.4	2.0	12	19	19	0	12	13	26	13	DX6 T5G
14	22.45	3 St.I	8	20	60	478	463	2	15	23.3		28.5	1.5	8	24	5	9	37	9	42	0	DX6 T5G
15	22.30	2 St.I	9	30	70	494	487	1	7	22.2		27.3	3.83	9	17	0	10	33	0	54	10	DX6 T5G
16	22.40	3 St.I	22	28	76	481	358	3	123	29.0		31.8	2.66	22	18	8	2	6	14	44	0	DX6 T5G
SUBJECT F.3		JULY - AUGUST 1965																				
1	22.40	3 St.I	15	19	146	500	485	3	15	29.5		22.3	3.0	15	0	3	37	1	17	45	5	AM. 10mg
2	22.50	1 St.I	18	19	181	490	472	4	18	19.0		16.5	4.5	18	0	0	1	5	33	6	33	AM. 10mg
3	23.00	0	17	20	122	480	466	6	14	23.5		20.0	3.66	17	0	2	6	28	4	31	22	AM. 10mg
	12.32	0	17	18	Awoke spontaneously																	
4	22.40	3 St.I	22	30	Record stopped after 60 mins.																	AM. 10mg

TABLE 3

Night	Start	D(Rem)	SOREM	d	D	TTB	TST	A	TA	III% ±	IV%	Rem%	Shift/ Hour	REM (mins) 1	2	3	4	5	6	7	8	TREAT-MENT
SUBJECT F.4	SEPT. - OCTOBER 1965																					
1	23.00	0	0	3	4	483	479	1	4	24.4		30.1	2.16	4	20	0	17	0	55	4	48	AM. 10mg
2	22.40	2. St.I	12	15	84	478	423	4	55	22.5		17.5	4.5	12	10	0	13	12	10	29	0	AM. 10mg
3	22.30	1. St.I	15	18	96	496	465	3	31	21.3		19.6	4.66	15	2	0	26	6	31	24	3	AM. 10mg
	12.30	3 AW/I	14		Awoke Spontaneously																	
4	22.40	0	20	26	104	479	468	2	11	26.7		25.6	2.33	20	0	15	23	33	27	2	0	AM 10mg T5G
5	22.30	1 AW/I	22	30	98	476	475	1	1	19.1		29.7	2.5	22	0	0	11	1	49	12	46	AM 10mg T5G
6	22.50	3 St. I	18	25	120	481	418	4	66	25.1		29.2	2.0	18	0	13	11	33	14	33	0	AM 10mg T5G
SUBJECT F.5	FEB. - APRIL 1966																					
1	22.45	0	0	5	70	491	427	8	59	20.6		29.3	6.66	0	10	35	0	28	16	21	15	NIL
2	23.00	4 AW/I	16	22	72	456	450	1	6	18.5		20.2	3.0	16	18	22	5	30	0	0	16	NIL
3	22.30	3. St. I	6	10	75	486	471	3	15	20.0		22.3	4.66	6	32	10	18	6	22	13	4	NIL
	17.30	2 St. I	5	Awoke at end of Rem period																		NIL
	01.30	1 St. I	36	40	Awoke after 3 mins. Stage II																	NIL
4	22.45	3 AW/I	19	24	Stopped record after 60 mins																	T5G
5	22.20	6 St. I	24	30	Stopped record after 60 mins																	T5G
6	22.40	5 St. I	20	32	73	484	470	2	14	23.4		31.3	4.0	20	10	32	6	28	16	20	15	T5G
7	22.50	4 St. I	6	12		Stopped record after 60 mins																Deseril 6mg
8	22.45	3 AW/I	18	24	66	472	470	1	2	24.6		31.1	5.0	18	21	16	18	32	8	22	11	DX6 T5G
9	22.36	2 AW/I	16	26	-	Stopped record after 60 mins																DX6 T5G
10	22.50	1 St. I	14	21	-	Stopped record after 60 mins																DX6 T5G
11	22.46	6 AW/I	10	18	50	490	476	3	14	21.6		24.8	4.33	10	25	16	21	31	0	0	15	DX6 T5G

TABLE 4

Night	Start	D(Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins) 1	2	3	4	5	6	7	8	Treatment
SUBJECT F.6		JULY 66 - APRIL 1967																			
1	22.29	11 AW/I	17	28	74	496	476	3	20	25.8	24.2	2.16	17	14	10	31	11	12	16	21	NIL
2	22.10	2 St. I	10	18	89	498	467	4	31	35.0	25.5	3.50	10	11	21	6	31	18	22	10	NIL
3	22.28	3 St. I	6	20	80	513	508	1	5	24.9	20.7	4.5	6	20	10	14	8	17	31	5	NIL
4	22.30	3 AW/I	16	26	-	Stopped record after 30 mins															
	12.40	5 St. I	13	19		Woken by nurse at 13.00 after 1 min Stage II sleep															NIL
	17.35	2 St. I	11	-		Woke spontaneously															
5	22.40	4 St. I	43	52	96	486	468	2	18	38.3	31.0	2.15	43	0	12	17	11	21	23	18	T. 5G
6	22.50	5 St. I	14	26	-	Stopped record after 60 mins. Slept in ward during even before recording															T. 5G
7	22.36	3 St. I	19	24	89	473	463	3	10	30.5	26.8	3.0	19	14	8	27	13	24	7	12	T. 5G
8	22.35	2 St. I	41	45	94	491	476	4	15	27.8	29.8	5.5	41	0	17	21	14	12	28	9	T. 5G
9	22.50	4 AW/I	11	19	92	486	466	2	20	22.3	24.9	5.66	11	11	21	8	27	4	16	18	NIL
10	22.40	2 St. I	18	24	115	473	463	3	10	20.5	25.5	3.66	18	0	17	21	10	14	18	20	Deseril x 4
11	22.35	3 St. I	33	41	84	498	477	4	21	27.3	23.3	3.0	33	0	7	21	40	2	28	0	Des x 4 T5G
12	22.50	2 St. I	14	19	90	482	476	1	6	25.8	30.5	4.66	14	10	21	17	37	8	28	10	DX4 T5G
13	22.30	1 St. I	12	14		Stopped recording after 90 mins															DX6 T5G
14	22.40	4 AW/I	9	15	85	486	474	3	12	24.6	26.0	5.0	9	14	21	16	10	32	11	10	DX6 T5G
15	22.20	2 St. I	19	23	-	Stopped record after 90 mins Stage III/IV															DX8 T5G
16	22.40	3 St. I	12	16	90	478	476	1	2	26.9	27.6	3.66	12	10	14	28	9	17	31	8	DX6 T5G
17	22.36	0	0	2	17	482	480	1	2	26.9	29.2	4.66	30	0	27	10	41	6	18	8	DX6 T5G
18	22.26	2 St. I	15	19		Stopped record after 20 mins Stage II sleep															DX6 T5G
19	22.30	3 AW/I	16	21	92	476	470	2	6	27.8	31.5	5.0	16	10	24	23	8	18	27	22	DX6 T5G
20	22.32	2 St. I	14	18	-	Stopped record after 60 mins.															
21	22.20	2 St. I	29	32	82	501	490	2	11	22.8	33.5	3.6	29	6	28	19	14	36	22	10	T. 5G only
22	22.31	2 St. I	11	16	81	496	488	4	8	18.6	26.6	6.33	11	20	17	31	8	17	5	21	Ritalin T5G
23	22.30	3 St. I	6	10	78	484	480	3	4	22.4	25.0	5.0	6	23	17	31	11	9	15	8	Ritalin
24	22.40	4 St. I	12	18	62	Stopped record after 90 mins															Ritalin T5G
25	22.30	3 St. I	16	22	80	476	457	4	19	23.6	30.9	3.66	16	12	21	18	26	12	16	20	T. 5G
26	22.20	4 St. I	17	25	72	482	476	2	6	22.5	30.3	4.0	17	18	22	16	20	11	30	10	5HTP
27	22.40	2 St. I	13	21	68	478	470	1	8	20.6	27.5	5.0	13	22	16	28	14	10	18	8	NIL

TABLE 5

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT F.7		OCTOBER 1966																			
1	22.45	5 AW/I	13	20	86	476	462	4	14	31.6	24.2	4.66	13	10	14	26	0	31	0	18	NIL
2	22.25	2 St. I	11	18	80	480	472	1	8	27.5	25.4	3.0	11	21	0	36	22	0	18	12	NIL
3	22.36	1 St. I	15	22	72	491	476	3	15	29.6	27.5	5.33	15	16	0	42	0	19	31	8	NIL
	12.40	7 AW/I	10	20		Awakened by nurse at 13.10 with lunch.															NIL
4	22.40	1 St. I	18	20		Stopped recording at 23.30															T5G
5	22.32	4 St. I	20	26	74	482	478	1	4	28.6	28.3	2.66	20	15	8	21	20	41	0	10	T5G
6	22.42	0	0	11	32	486	451	7	24	22.4	24.4	5.66	10	12	30	0	40	0	0	18	Ritalin
7	22.36	0	0	7	48	492	471	3	14	25.6	24.0	4.66	12	21	0	36	0	17	10	18	Ritalin
8	22.26	1 St. I	14	18	76	481	476	1	5	26.4	25.6	3.66	14	16	21	0	17	18	21	15	Ritalin T5G
SUBJECT F.8		DECEMBER 1966 - JANUARY 1967																			
1	22.30	0	0	51	66	465	410	2	4	36.1	17.2	2.66	0	14	17	2	23	15	0	-	Ritalin Fenta
2	22.35	0	0	54	54	478	423	1	1	22.5	19.1	4.5	4	2	13	0	38	0	28	-	" "
3	22.28	4 AW/I	6	20	94	476	452	2	24	20.8	21.2	3.0	6	16	21	1	21	3	16	18	" "
4	22.40	3 St. I	10	23	101	483	449	4	34	19.3	27.0	4.0	10	7	0	19	13	12	47	13	" "
	12.20	6 AW/I	14	25		Woke spontaneously after 4 mins. Stage II sleep															" "
5	22.40	4 St. I	15	26	62	496	465	3	31	21.3	26.2	4.66	15	11	3	29	6	31	24	3	Rit. T5G Fent
6	22.32	2 St. I	11	18	39	482	477	1	5	22.4	20.8	3.33	14	10	24	0	42	1	8	-	Rit. T5G Fent
7	22.30	6 AW/I	14	24	72	481	417	6	64	29.1	30.7	2.0	14	12	19	11	33	14	33	0	Rit. T5G Fent

TABLE 6

Night	Start	D(Rem)	SOREM	d	D	TTB	TST	A	TA	III% +	IV%	REM%	Shifts/ Hour	REM (mins) 1	2	3	4	5	6	7	8	Treatment
SUBJECT F.9		JANUARY 1967																				
1	22.50	0	0	23	94	494	460	2	11	22.2		26.7	2.66	0	13	19	0	27	31	4	29	AM. 15mg
2	22.32	0	0	14	45	484	458	3	12	24.3		22.5	3.66	15	10	17	21	0	30	0	10	AM. 15mg
3	22.36	2 St.I	3	11	44	486	472	2	14	23.6		29.9	2.0	16	5	20	11	16	29	14	30	AM. 15mg
4	22.40	3 AW/I	8	15	82	490	482	1	8	20.6		24.9	4.33	8	26	15	0	42	0	13	16	AM. 15mg
	12.36	0	0	2		No REM sleep in 24 mins. total sleep.						Woken by Nurse										AM. 15mg
	12.20	2 St. I	4	6		Woke spontaneously after 14 mins																AM. 15mg
5	22.34	1 St. I	14	20	75	486	462	3	24	28.4		27.5	4.0	14	21	8	16	0	36	11	21	AM. 15mg
SUBJECT F.10		MARCH - APRIL 1967																				
1	22.20	0	0	24	90	486	436	6	26	12.8		22.7	5.0	0	15	0	20	17	3	28	16	Ritalin
2	22.50	0	0	10	66	480	455	3	15	14.9		29.2	4.0	0	21	14	8	16	23	30	21	Ritalin
3	22.47	0	0	16	82	479	456	1	7	13.0		25.7	3.66	0	16	0	26	22	17	26	10	Ritalin
4	22.40	0	0	8	77	-	Stopped after first cycle of sleep 00.10															Ritalin
5	22.30	0	0	3	50	-	Stopped after first cycle of sleep 23.30															Ritalin
6	22.70	6 AW/I	2	9	82	484	472	3	12	14.0		29.0	4.0	2	26	31	0	42	0	17	19	Ritalin
	12.30	5 St. I	4	9		Woke after 2 min Stage II sleep																Ritalin
7	22.20	4 St. I	9	15	76	480	468	4	12	16.8		29.1	3.66	9	12	17	29	14	36	0	9	Ritalin T5G
SUBJECT F.11		OCTOBER - DECEMBER 1967																				
1	22.40	0	0	20	69	482	460	2	2	22.7		20.8	3.83	0	5	10	16	18	0	18	29	AM. 15mg
2	22.31	0	0	12	58	482	470	0	0	31.1		20.4	3.33	1	8	16	0	23	9	33	7	AM. 15mg
3	22.42	2 AW/I	11	22	100	489	469	2	20	22.9		27.7	5.00	11	13	0	20	18	30	0	38	AM. 15mg
4	22.35	4 AW/I	13	26	86	483	470	2	13	27.5		27.8	4.63	13	12	15	8	2	0	25	32	AM. 15mg
	12.40	4 St. I	14	20		Awoke after 1 min Stage II sleep																
5	22.45	2 St. I	22	31	84	484	476	2	8	29.8		28.2	5.33	22	3	24	10	22	2	45	6	AM. 15mg T5
6	22.40	4 St. I	18	25	122	482	478	1	4	27.4		27.0	4.00	18	0	17	25	3	33	15	18	AM. 15mg T
7	22.31	3 St. I	20	24	80	500	486	3	14	21.4		28.2	3.83	20	15	10	12	10	24	20	26	AM. 15mg T
8	22.35	5 St. I	24	30	79	484	480	1	4	26.8		25.2	4.16	24	9	11	10	17	13	3	24	AM. 15mg T

APPENDIX II. IDIOPATHIC NARCOLEPSY B. MALE SUBJECTS TABLE I.

Night	Start	D(Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hours	REM (mins) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.1 MAY - OCTOBER 1964																					
1	22.20	2 AW/I	11	20	75	488	461	6	27	18.8	16.3	5.33	11	21	16	8	0	22	18	10	NIL
2	22.38	4 AW/I	13	19	64	Stopped record after 90 mins.															NIL
3	22.42	3 AW/I	10	15	70	472	450	4	22	16.0	27.6	4.0	10	26	0	18	22	16	30	0	NIL
	12.50	1 AW/I	11	14		Woke spontaneously after 6 mins. Stage II sleep															NIL
4	22.50	0	19 nightmare			Woke out of nightmare. Refused to sleep in laboratory															T5G
5	22.45	3 St. I	12	16		Woken by me after 30 mins. and returned to Ward. Would not spend night in laboratory															T5G
6	22.30	2 St. I	26			Woke out of nightmare and returned to Ward															T5G
7	22.45	0	6	9		Woken after 60 mins.															Deseril X3
8	22.40	0	11	14		Woken after 60 mins.															Deseril X3
9	22.36	0	23	26		Woken after 60 mins.															Deseril X6
	12.40	1 AW	0	1	49	Slept (Stage II & III) for 44 mins. Woke spontaneously															Deseril X6
	12.32	1 St. I	13	-		Woke spontaneously at end of REM sleep															Ascorbic aci
10	22.40	4 St. I	16	22		Woken after 60 mins.															NIL
11	22.45	3 St. I	23	26		Woken at 60 mins.															NIL
12	22.36	0	0	7		Woken at 60 mins. Had slept in ward before recording															T5G
13	22.50	13 AW/I	15	30		Woken at 60 mins.															NIL
14	22.40	6 St. I	25			Woke out of nightmare															T5G
15	22.36	4 St. I	26			Woke spontaneously. Described 'Vivid' dream															T5G
16	22.50	3 St. I	10	15		Woke at 60 mins.															Tofranil 25m
17	22.46	4 St. I	2	6		Woke at 60 mins.															Tof. 75mg T
18	22.40	6 St. I	12			Woke spontaneously from REM sleep															Tof. 75mg T
19	22.36	7 St. I	8	20		Woke after 60 mins.															Tof. 75mg T
20	22.40	4 St. I	3	8		Woke at 60 mins.															Tof. 75mg T
21	22.46	3 St. I	11	15		Woke at 60 mins.															Tof. 75mg T
22	22.36	8 St. I	10	20		Woken at 60 mins.															Tof. 75mg T

APPENDIX II.

TABLE II

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M. 2		JANUARY - MARCH 1965																			
1	22.50	0	0	17	68	460	432	2	11	23.4	21.1	2.50	0	17	0	25	0	29	8	12	AM. 15mg
2	23.00	0	0	42	78	509	467	0	0	20.8	25.9	2.16	0	26	0	24	7	15	49	0	AM. 15mg
3	22.30	6 AW/I	8	19	124	492	473	0	0	19.0	18.0	2.50	8	0	9	9	16	14	6	31	AM. 15mg
4	22.40	4 AW/I	15	19	105	494	471	1	23	19.0	16.8	2.83	15	0	4	0	49	0	23	2	AM. 15mg
	12.39	3 AW/I	17	24		Awoken by Nurse at 13.00															AM. 15mg
	12.40	0	15	-		Awoke from REM sleep															AM. 15mg
5	22.30	0	12	15	75	500	489	2	11	26.6	26.6	3.66	12	2	3	0	24	11	60	8	Off 4 days
6	22.40	0	27	30	63	494	477	1	17	25.6	27.2	3.00	27	3	17	10	1	17	48	5	Off 6 days
7	22.41	0	0	18	70	494	471	1	5	22.2	25.9	2.50	0	17	0	10	31	0	54	10	Deseril X6
8	22.50	0	0	14	78	481	467	0	0	20.8	26.3	2.16	0	26	0	24	9	15	19	0	Des X6 T5G
9	22.42	0	0	11	85	479	468	0	0	26.7	27.8	2.33	0	35	20	3	33	27	12	0	Des X6 T5G
10	22.30	0	0	5	84	483	478	0	0	20.3	20.5	3.33	0	2	3	37	15	7	28	6	Des X6 T5G
11	22.45	4 AW/I	18 (nightmare)	25	62	476	452	3	24	20.8	21.2	3.00	18	16	3	1	21	3	16	18	NIL
12	22.40	3 St. I	26	30	91	483	449	4	34	19.3	24.7	4.00	26	0	11	0	2	12	47	13	T5G
13	22.30	4 St. I	31 (nightmare)	40	61	510	459	6	51	28.6	21.6	5.66	31	2	0	2	9	6	49	0	T5G
14	22.45	3 St. I	30 (")	52	86	483	429	1	54	28.3	24.3	2.00	30	0	0	10	20	35	0	9	T5G
15	22.30	2 St. I	12	20	78	484	467	3	17	22.8	25.9	4.16	12	14	0	26	0	20	47	2	NIL

TABLE III

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.3 MAY - OCTOBER 1965																					
1	22.50	1 St. I	2	4	70	483	470	3	13	18.6	23.6	4.00	12	18	16	27	13	32	10	8	NIL
2	22.42	3 AW/I	11	15	75	478	461	2	17	16.0	28.4	2.00	11	26	14	21	27	23	20	0	NIL
3	22.30	4 AW/I	10	16	Stopped at 60 mins																NIL
4	22.40	0	0	20	80	Stopped at 120 mins. Had slept on journey to Laboratory															NIL
5	22.39	4 St. I	4	10	70	491	480	2	11	17.6	20.9	3.66	4	28	11	16	22	13	29	10	NIL
	12.56	2 St. I	11	14	Woken by Nurse at 13.15																NIL
	12.50	1 St. I	5	6	Woken by Nurse at 13.00																NIL
6	22.50	1 St. I	30	33	60	Stopped after 90 mins.															T5G
7	22.45	1 St. I	34	36	70	Stopped at 90 mins.															T5G
8	23.00	4 AW/I	15	20	Stopped at 60 mins.																NIL
9	22.45	2 AW/I	38	40	96	486	470	3	16	20.4	33.2	3.0	38	0	17	26	28	14	10	21	T5G
10	22.53	3 St. I	43	52	Stopped at 60 mins.																T5G
11	22.40	4 AW/I	17	20	Stopped at 60 mins.																NIL
12	22.30	6 AW/I	14	26	Stopped at 60 mins.																NIL
13	22.45	6 AW/I	54	70	Stopped at 90 mins.																T5G
14	22.36	5 AW/I	19	24	Stopped at 60 mins.																Deseril x6 T
15	22.39	4 AW/I	78	82	Stopped at 90 mins.																Des. X6 T5G
16	22.40	6 AW/I	28	36	Stopped at 60 mins.																Des. X6 T5G
17	22.39	4 AW/I	39	43	Stopped at 60 mins.																Des. X6 T5G
18	22.40	6 St. I	39	50	Stopped at 60 mins.																Des. X6 T5G
19	22.45	4 St. I	22	28	Stopped at 60 mins.																Des. X6 NIL
20	22.50	2 St. I	12	14	Stopped at 60 mins.																Des. X6 NIL

TABLE IV

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.4		NOVEMBER 1965 - JANUARY 1966																			
1	22.50	0	0	21	65	482	456	1	5	22.4	19.3	3.33	0	10	24	3	42	1	8	0	AM. 15mg
2	22.40	0	0	14	44	478	423	3	41	22.5	19.4	4.50	4	2	13	0	38	0	29	0	AM. 15mg
3	22.50	0	0	20	37	460	356	4	84	28.6	18.8	4.33	10	0	10	15	12	0	30	-	AM. 15mg
4	22.40	3 St. I	6	15	30	496	465	3	31	21.3	22.6	4.66	9	29	6	31	24	11	0	3	AM. 15mg
5	22.40	2 St. I	8	16	68	483	449	2	34	19.3	24.7	4.00	8	7	0	19	13	12	47	13	AM. 15mg
	12.30	4 AW/I	15	20		A woken by Nurse at 13.00															AM. 15mg
6	22.40	5 St. I	20	30	68	483	478	1	5	20.3	23.4	3.33	20	2	3	31	15	7	28	6	AM. 15mg T
7	22.20	4 AW/St.I	24	32	106	482	477	1	5	22.4	24.1	3.00	20	0	18	20	15	30	16	32	AM. 15mg T
8	22.40	3 St.I	16	19	100	481	474	1	7	22.7	24.1	4.50	16	1	11	18	17	32	4	15	AM. 15mg T
9	22.50	5 St. I	18	26	166	476	473	1	3	19.0	29.0	2.50	18	0	0	9	19	42	6	42	AM. 15mg T
10	22.30	1 St. I	15	30	89	478	475	1	3	19.6	29.7	3.00	15	1	8	25	0	18	37	37	NIL Off 1 da
11	22.35	5 St. I	21	36	92	481	358	6	123	29.0	39.9	5.66	21	18	18	2	26	14	44	0	Off 3 days
12	22.40	6 AW/I	18	32	60	486	468	3	18	33.8	30.9	2.50	18	20	5	10	37	20	15	19	Off 15 days
13	22.30	3 St. I	10	20	56	482	416	2	62	29.8	26.2	2.33	10	15	19	0	20	0	28	17	Deseril X6
14	22.40	2 St. I	12	22	55	483	468	1	15	33.8	27.4	2.50	12	20	5	10	27	10	15	29	Des x6 T5G
15	22.45	3 St. I	15	24	71	482	398	4	84	23.5	21.4	2.33	15	17	17	10	13	0	0	13	Des x6 T5G
SUBJECT M.5		OCTOBER - DECEMBER 1966																			
1	22.27	-	-	7	95	499	431	4	68	21.4	25.3	3.83	0	15	0	12	10	24	20	29	AM. 15mg
2	22.30	4 St. I	20	30	143	482	478	1	4	27.4	22.6	4.00	20	0	7	30	6	32	15	18	AM. 15mg
3	22.40	3 St. I	14	22	94	480	476	1	4	29.8	23.1	5.33	14	3	24	7	22	3	45	6	AM. 15mg
4	22.30	2 St. I	32	40	90	474	458	3	16	29.4	27.7	6.33	32	2	17	6	10	42	9	9	Off 3 days
5	22.41	3 St. I	28	38	96	483	474	1	9	36.5	30.2	4.63	28	3	22	15	10	21	14	29	Off 6 days
6	22.40	4 St. I	25	36	84	486	470	3	16	27.4	26.9	3.83	25	4	15	8	2	10	25	32	Off 10days
7	22.50	3 St. I	16	25	72	473	469	1	4	27.6	22.6	3.33	16	3	10	25	19	10	23	0	Off 13 days

TABLE V

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	111% + IV%	Rem%	Shifts/ Hour	REM (min) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.5		(cont'd)																			
8	22.50	1 St. I	33	36	64	489	469	2	20	22.9	31.8	5.00	33	13	0	20	18	30	0	35	T5G
9	22.32	2 St.I	28 (nightmare)	35	70	482	460	3	12	22.7	27.4	3.83	28	5	10	16	18	0	19	30	T5G
10	22.40	3 St. I	27	40	92	483	452	4	31	28.1	26.1	4.16	27	0	17	0	24	10	30	10	T5G
11	22.30	1 St. I	8	20	120	482	458	3	24	29.9	22.5	4.83	8	0	19	10	15	16	10	25	Des x 6
12	22.40	4 St. I	14	26	74	482	470	2	12	31.1	25.5	3.33	14	7	17	10	23	9	33	7	Des x6 T5G
13	22.30	3 St. I	12	18	120	484	480	1	4	26.8	24.4	4.16	12	0	19	10	15	16	10	25	Des x6 T5G
14	22.40	5 St. I	15	25	62	483	472	2	11	26.5	26.9	4.63	15	2	22	15	10	20	14	29	Des x6 T5G
15	22.40	6 St. I	11	21	130	489	459	4	30	28.1	22.4	6.16	11	0	7	10	25	10	30	10	NIL
	12.40	1 St. I	9	0	Woke spontaneously from REM sleep																NIL
SUBJECT M.6		MARCH 1967																			
1	22.33	0	? 1	7	32	496	482	2	14	20.4	29.5	3.66	28	12	27	10	42	0	16	8	AM. 15mg
2	22.50	0	? 1	8	50	Stopped record at 60 mins.															AM. 15mg
3	22.40	0	0	6	45	Stopped record at 60 mins.															AM. 15mg
4	22.30	0	? Traces	2	60	499	490	2	9	21.6	24.3	4.00	0	12	26	22	0	28	31	0	AM. 15mg
	12.25	3 St. I	1	6	Slept for 20 mins and woke spontaneously																AM. 15mg
	18.30	4 AW/St.I	2	9	Woke after 15 mins.																AM. 15mg
5	22.41	3 St. I	0	4	92	Stopped at 120 mins.															AM. 15mg T
6	22.26	2 St. I	3	6	86	511	506	2	5	24.8	36.0	3.66	3	26	41	0	30	11	25	10	AM. 15mg T
7	22.40	6 AW/I	1	7	Stopped after 60 mins.																AM. 15mg. T

TABLE VI

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M. 7		JULY 1967																			
1	22.53	5 AW/I	16	24	90	468	457	1	11	18.6	16.2	3.66	16	8	14	10	0	29	0	13	AM. 15mg
2	22.35	3 AW/I	4	10	51	492	481	2	11	20.9	22.5	4.66	4	26	10	0	21	15	21	0	AM. 15mg
3	22.40	4 AW/I	10	20		Stopped record at 90 mins.															AM. 15mg
	17.41	3 AW/I	2		Woke abruptly after 5 mins																AM. 15mg
	17.35	1 St. I	10	12		Woke spontaneously after 3 mins. Stage II sleep															AM. 15mg
4	22.40	2 St. I	6	13	.92	Stopped after 120 mins. recording															AM. 15mg T5
5	22.26	2 St. I	3	6	86	487	461	5	26	22.6	26.7	5.33	10	31	16	0	17	21	18	10	AM. 15mg T5
6	22.50	5 St. I	18	25		Stopped record at 90 mins.															AM. 15mg T5
SUBJECT M. 8		JULY 1967																			
1	22.30	0	0	2	50	510	473	8	37	11.4	23.5	7.66	10	20	0	42	0	13	16	10	AM. 10mg
2	22.42	0	0	6	42	Stopped record after 90 mins.															AM. 10mg
3	22.30	3 St. I	11	15	60	498	490	2	8	12.6	26.1	4.66	11	32	10	17	8	26	11	23	AM. 10mg
	12.36	4 St. I	6	Woke at end of Rem sleep																	AM. 10mg
4	22.50	2 St. I	12	15		Stopped recording at 60 mins															AM. 10mg T5
5	22.45	3 St. I	14	21		Stopped recording at 80 mins															AM. 10mg T5
SUBJECT M. 9		JULY 1967																			
1	22.20	6 St. I	15	30	70	499	486	2	13	21.4	25.9	3.83	15	15	0	12	10	24	20	30	NIL
2	22.32	5 St. I	12	20	92	480	476	1	4	29.8	26.5	5.33	12	3	24	10	21	2	45	6	NIL
3	22.30	2 St. I	16	22	91	482	480	1	4	26.8	22.9	4.16	16	9	13	11	10	17	13	24	NIL
	12.32	4 St.	14	20		Woken by nurse at 13.00															NIL
4	22.40	1 St. I	22	26	72	483	474	2	9	25.5	26.6	6.33	22	11	13	10	21	7	22	20	T5G
5	22.41	2 St. I	26	32	85	473	469	1	4	39.2	29.4	3.33	26	3	14	24	19	20	22	20	T5G
6	22.39	6 St. I	18	30	106	477	467	2	10	26.3	29.6	5.10	18	0	21	10	24	23	32	10	T5G

TABLE VII

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M10		DECEMBER 1967																			
1	22.40	5 AW/I	11	19	72	520	502	3	18	29.6	25.9	5.66	11	17	21	36	0	27	0	18	NIL
2	22.36	0	0	5	50		Stopped at end of first cycle of sleep														NIL
3	22.30	3 St. I	10	14	90		Stopped at end of first cycle of sleep														NIL
	12.40	4 St. I	6	11			Woken by nurse at 13.00														NIL
4	22.40	1 St. I	17	30	72	500	492	1	8	30.6	30.8	4.66	17	20	31	0	18	32	16	18	T5G
SUBJECT M. 11		APRIL 1968																			
1	22.42	3 St. I	2	8	86		Stopped after end of first cycle of sleep														AM. 15mg
2	22.30	0	0	2	55	484	480	1	2	12.6	26.7	3.66	5	30	0	14	21	17	31	10	AM. 15mg
3	22.45	3 St. I	11	16	70	496	474	4	22	12.8	28.9	4.00	11	29	13	36	0	38	10	30	AM. 15mg
	12.26	4 St. I	2		Woke abruptly from REM sleep																AM. 15mg
4	22.40	2 St. I	14	16	Stopped after 60 mins.																AM. 15mg T5(
5	22.36	6 St. I	4	15	Stopped at 60 mins.																AM. 15mg T5(
6	22.40	1 St. I	18	20	78	480	470	2	10	14.6	26.8	3.00	18	20	14	0	36	0	28.	10	AM. 15mg T5(
SUBJECT M. 12		MAY 1968																			
1	22.40	2 St. I	12	20	104	472	468	1	4	38.1	26.7	2.00	12	0	11	18	8	24	21	31	AM. 15mg
2	22.36	3 AW/I	14	22	102	468	466	1	2	21.6	24.0	2.33	14	10	12	11	10	34	11	10	AM. 15mg
3	22.50	5 St. I + 1 St. II	16	30	68	476	476	0	0	38.2	32.7	1.62	16	19	16	21	16	27	32	6	AM. 15mg
4	22.42	3 St. I	8	15		468	468	0	0	38.0	28.6	2.33	8	10	10	17	8	18	22	41	AM. 15mg
	12.41	5 St. I	12		Woke spontaneously 2 mins after last eye movement																AM. 15mg
5	22.38	1 St. I	18	24	82	461	459	1	2	30.7	30.9	1.50	18	12	29	10	29	13	12	19	AM. 15mg T5(
6	22.40	2 St. I	24	31	78	459	450	2	9	35.7	33.3	3.00	24	18	11	10	42	6	33	6	AM. 15mg T5(
7	22.51	1 St. I	20	21	89	461	440	3	21	39.1	32.1	2.63	20	11	19	24	27	16	24	10	AM. 15mg T5(
8	22.30	3 St. I	16	20	29	462	450	2	12	35.7	36.0	3.00	27	8	12	10	42	6	33	24	AM. 15mg T5(

TABLE VIII

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M. 13		APRIL 1969																			
1	22.40	2. St. I	14	20	81	480	477	1	3	22.4	21.4	3.33	14	13	24	0	42	1	8	0	NIL
2	23.13	1 St. I	10	13	147	479	431	13	47	20.9	21.7	6.33	10	0	18	0	1	27	10	24	NIL
	12.40	3 St. I	13	18		Awoke spontaneously after 6 mins Stage II sleep															
3	22.31	4 St. I	22	31	72	476	452	11	24	26.8	33.0	4.33	22	16	22	11	21	13	16	28	T5G
4	22.40	3 St. I	20	28	78	483	477	4	6	26.6	29.5	4.66	20	6	23	22	10	21	17	22	T5G
SUBJECT M. 14		APRIL - MAY 1969																			
1	22.50	5 AW/I	6	13	78	486	472	2	14	30.6	27.7	4.66	6	21	16	22	4	41	13	8	NIL
2	22.45	7 AW/I	4	15	70	480	476	1	4	28.4	27.5	4.00	4	31	20	0	14	30	12	21	NIL
3	22.50	0	0	3	90	478	475	0	0	22.4	22.1	2.00	0	30	16	0	41	0	10	8	NIL
	12.40	3 AW/I	13		Awoke at end of REM sleep																NIL
4	22.40	1 St. I	16	18	76	480	477	1	3	25.6	25.6	3.00	16	18	21	0	17	23	14	10	T5G
5	22.32	3 St. I	12	18	70		Stopped record after 90 mins.														T5G
SUBJECT M. 15		JUNE - JULY 1969																			
1	22.39	4 St. I	27	41	97	520	487	14	33	26.2	28.1	6.00	27	0	18	0	29	0	39	24	NIL
2	22.40	2 St. I	12	18	90	476	475	1	1	19.1	32.0	2.50	12	12	10	21	11	48	12	26	NIL
3	22.41	1 St. I	30	40	40	470	468	1	2	26.7	34.2	3.33	30	35	20	3	33	27	2	10	T5G
4	22.31	2 St. I	36	45	55	480	479	1	1	24.4	36.3	3.00	36	20	10	21	0	55	4	48	T5G
5	22.40	0	0	4	88	530	517	3	9	28.6	29.4	3.66	0	14	0	28	33	38	0	39	Tofranil 50m
6	21.51	0	0	11	369	537	459	11	67	19.4	15.3	6.33	0	0	0	0	0	0	24	46	Tofranil 50m
7	21.42	0	0	24	51	466	442	4	24	20.2	24.2	4.5	0	23	7	24	15	25	13	0	Tofranil 50m
	12.32	4 St. I	14	20		Awoken by nurse at 13.00															NIL

TABLE IX

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	111%	+IV%	Rem%	Shifts/ Hour	REM (Mins). 1	2	3	4	5	6	7	8	Treatment
SUBJECT M. 16 NOVEMBER 1969 - JANUARY 1970																						
1	23.30	4 AW/I	6	14	72	430	417	3	13	20.4		31.9	4.00	6	17	24	28	16	10	12	18	NIL
2	23.10	6 AW/I	10	18	84	448	430	2	18	21.6		23.7	5.33	10	8	16	22	14	0	11	21	NIL
3	22.50	3 St. I	19	16		Stopped record at 60 mins																NIL
	12.50	2 St. I	6	9		Woken at 13.00 by nurse																NIL
4	22.42	0	0	16	50	486	459	1	11	20.0		25.3	4.66	10	17	21	8	19	11	30	10	Tofranil 75m
5	22.40	6 St. I	2	8	47	480	476	1	4	22.6		28.2	5.00	13	21	16	10	9	23	29	16	Tofranil 75m

APPENDIX II. PART C. SYMPTOMATIC NARCOLEPSY TABLE 1

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.1 FEBRUARY 1965																					
1	22.30	0	0	20	80	480	426	6	34	13.6	16.0	5.00	0	10	0	0	15	22	5	16	NIL
2	22.50	0	0	45	96	500	435	3	20	15.6	25.7	4.66	0	0	26	0	15	29	15	27	NIL
3	22.30	0	0	36	102	510	420	18	54	14.8	18.8	4.00	0	0	20	0	6	26	18	9	T5G
	12.30	0	0	Drowsy		No sleep spindles															NIL
	12.42	0	0	15			Slept very well. Few sleep spindles														NIL
SUBJECT M.2 JULY 1965																					
1	22.40	0	0	90	280	500	272	26	138	6.6	28.7	8.00	0	0	0	0	0	0	36	42	NIL
2	22.30	0	0	96	176	484	300	16	88	8.8	28.0	5.66	0	0	0	0	16	22	8	38	NIL
3	23.10	0	0	62	154	470	310	4	98	7.0	27.4	4.00	0	0	0	10	17	36	14	8	T5G
4	23.00	0	0	51	168	474	530	12	93	6.1	28.5	5.00	0	0	0	20	0	33	27	14	NIL
	12.25	0	0	Drowsy but no sleep																	NIL
	12.36	0	0	Prolonged drowsiness																	NIL
	17.20	0	0	20		Slept10 mins. Stage II															NIL
	19.30	0	0	15		Slept 30 mins. Stage II															NIL
SUBJECT M.3 SEPTEMBER 1967																					
1	22.40	0	0	10	136	600	494	8	96	33.6	23.5	4.66	0	0	10	21	27	11	16	32	NIL
2	22.30	0	0	16	127	510	470	3	24	32.8	22.8	3.00	0	0	25	17	20	0	31	14	NIL
3	22.35	0	0	20	110	510	466	2	24	36.4	20.2	3.66	0	0	31	0	27	15	11	10	T5G
4	22.30	0	0	16	135	510	474	3	20	38.4	19.4	4.00	0	0	28	10	17	21	0	15	NIL
	12.30	0	0	Persistent drowsiness																	NIL
	12.35	0	0	16		10 mins. Stage II sleep															NIL
	17.30	0	0	5		30 mins. Stage II sleep															NIL
	19.30	0	0	10		60															NIL

Slept for 80 mins. 8 mins. REM Sleep

TABLE 2

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	111% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.4		MARCH 1968																			
1	22.40	0	0	5	90	500	490	1	5	42.6	16.7	2.00	0	21	0	14	16	0	31	0	NIL
2	24.46	0	0	4	68	494	490	0	0	40.3	20.6	2.66	0	26	10	6	18	0	41	0	NIL
3	22.50	0	0	6	70	490	484	0	0	36.7	21.3	1.00	0	10	31	0	11	19	32	0	T5G
4	22.45	0	0	7	91	488	481	0	0	39.6	23.7	1.66	0	16	21	14	27	0	36	0	NIL
SUBJECT F.1		MARCH - MAY 1966																			
1	22.30	6 AW/I	1mins	8	120	510	474	4	36	11.8	17.1	3.66	1	0	10	14	21	11	16	8	NIL
2	22.45	0	0	10	114	500	476	2	14	13.6	17.4	4.00	0	6	27	0	14	8	28	0	NIL
3	22.40	7 AW/St.I	1	9	126	500	456	5	44	12.8	25.0	3.0	1	0	28	11	16	21	27	10	T5G
4	22.51	6 AW/I	1	8	116	490	471	3	19	11.8	21.4	4.66	1	0	10	21	0	17	38	15	T5G
	12.20	0	0		Drowsy only																NIL
	12.36	8 AW/I	?		Woke spontaneously																NIL
	13.00	6 AW/I	1	8	Woke spontaneously after 20 mins Stage II sleep																NIL
SUBJECT F.2		APRIL - JULY 1967																			
1	22.35	0	0	40	56	505	379	6	86	10.9	25.9	5.66	0	21	0	16	18	22	5	16	NIL
2	22.40	0	0	36	92	500	416	4	58	13.9	25.5	4.00	0	0	36	0	17	19	21	13	NIL
3	22.45	0	0	21	102	495	429	3	45	12.6	21.9	4.66	0	0	31	11	21	0	31	0	T5G
4	22.40	0	0	26	68	500	430	4	44	11.0	23.7	3.33	0	21	0	33	0	11	16	21	NIL
	12.20	0	0	Drowsy only																	NIL
	12.30	0	0	Drowsy only																	NIL
	17.26	0	0	Drowsy only																	NIL
	19.40	0	0	16	Slept 25 mins. Stage II sleep																NIL

APPENDIX II. SECTION D. CONTROL SUBJECTS TABLE 1

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (Mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT F.1 (AET 37)																					
1	22.40	0	0	13	90	482	439	3	30	14.3	20.1	3.33	0	7	13	3	29	12	13	5	NIL
2	23.20	0	0	20	87	440	420	0	0	20.7	22.4	3.63	0	10	22	0	26	4	22	10	NIL
	12.40	0	0	16	Slept 4 mins. (Stage II)																NIL
	17.40	0	0	10	Slept 24 mins. (Stage II + III)																NIL
SUBJECT F.2 (AET 24)																					
1	23.40	0	0	9	64	452	441	1	2	31.6	16.5	4.00	0	18	14	0	18	14	16	0	NIL
2	23.22	0	0	12	126	486	484	0	0	26.4	25.6	2.66	0	0	26	14	16	35	14	21	NIL
	12.32	0	0	Drowsy. No sleep spindles																	NIL
	12.40	0	0	10	5 mins. Stage II sleep																NIL
SUBJECT F.3 (AET 40)																					
1	22.59	0	0	29	79	485	406	4	50	14.8	22.9	3.66	0	21	0	26	0	11	25	0	NIL
2	23.10	0	0	10	84	470	456	1	4	16.0	29.2	3.00	0	20	15	30	0	22	26	10	NIL
	12.40	0	0	Drowsy only																	NIL
	12.50	0	0	Drowsy																	NIL
SUBJECT F.4 (AET 42)																					
1	22.50	0	0	20	72	490	451	2	19	11.8	13.5	4.66	0	22	0	18	0	21	0	0	NIL
2	23.00	0	0	15	90	480	460	1	5	9.8	20.9	3.00	0	15	7	27	8	21	10	8	NIL
	12.30	0	0	10	10 mins. Stage II sleep																NIL
	12.42	0	0	15	6 mins. Stage II sleep																NIL
SUBJECT F.5 (AET 26)																					
1	22.45	0	0	31	64	475	438	3	6	28.9	16.3	4.00	0	3	0	17	9	0	29	13	NIL
2	23.00	0	0	17	94	465	447	1	1	21.1	21.7	3.66	0	14	0	16	13	30	4	20	NIL
	12.35	0	0	16	Slept 9 mins. (Stage II)																NIL
	12.30	0	0	10	Slept 15 mins (Stage II)																NIL

TABLE 2

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT E.6	(AET 36.)																				
1	23.00	0	0	10	120	480	462	2	8	14.8	20.8	3.66	0	0	26	24	10	0	28	10	NIL
2	23.10	0	0	15	100	470	455	0	0	15.6	25.7	2.00	0	10	22	31	0	26	20	8	NIL
	12.40	0	0	Drowsy only																	NIL
	12.30	0	0	15	Slept 5 mins. Stage II sleep																NIL
SUBJECT F.7	(AET 29)																				
1	23.30	0	0	11	95	475	428	8	36	18.5	24.0	6.16	0	5	0	22	2	37	33	3	NIL
2	23.10	0	0	9	83	472	463	0	0	27.9	24.4	3.33	0	5	0	30	11	16	38	13	NIL
SUBJECT F.8	(AET 27)																				
1	22.50	0	0	30	64	466	436	0	0	22.6	19.1	3.50	0	8	9	17	13	26	10	0	NIL
2	22.59	0	0	9	66	482	467	3	5	14.0	23.6	4.00	0	10	11	17	5	34	2	32	NIL
	12.30	0	0	5	Slept 15 mins. (Stage II)																
	12.41	0	0	15	Slept 5 mins only (Stage II)																
SUBJECT M.1	(AET 36)																				
1	23.00	0	0	35	79	485	406	6	44	15.2	22.9	4.66	0	31	0	26	0	11	25	0	NIL
2	22.50	0	0	26	78	480	436	2	18	16.8	22.9	3.00	0	26	14	22	8	10	20	0	NIL
	12.42	0	0	Drowsy only																	NIL
	12.30	0	0	6	Slept 20 mins. (Stage II)																NIL
SUBJECT M.2	(AET 38)																				
1	22.50	0	0	14	90	490	448	3	28	14.0	19.4	4.33	0	21	8	26	0	14	18	0	NIL
2	23.00	0	0	20	72	480	456	1	4	15.2	24.6	3.00	0	28	0	30	8	21	22	3	NIL
	12.40	0	0	16	Slept 4 mins. (Stage II)																NIL
	12.32	0	0	10	Slept 18 mins. (Stage II)																NIL

TABLE 3

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (Mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.3	(AET 56)																				
1	22.50	0	0	30	150	455	400	2	25	11.6	22.5	5.66	0	0	0	30	0	36	14	10	NIL
2	22.45	0	0	25	120	480	450	1	5	10.8	23.3	4.00	0	0	36	0	12	21	26	10	NIL
	12.40	0	0	Drowsy only																	NIL
	17.30	0	0	15		Slept 40 mins. (Stage II)															NIL
SUBJECT M.4	(AET 26)																				
1	23.10	0	0	19	125	444	418	1	7	23.4	19.4	4.83	0	9	0	7	13	6	46	0	NIL
2	23.15	0	0	17	83	462	445	0	0	23.5	22.4	5.33	0	10	0	13	11	15	27	28	NIL
	12.30	0	0	16		Stage II Sleep for 10 mins															NIL
	12.40	0	0			Drowsy only															NIL
SUBJECT M.5	(AET 22)																				
1	23.30	0	0	40	48	464	404	2	20	20.3	24.6	4.50	9	0	36	0	32	6	16	0	NIL
2	23.42	0	0	89	58	462	370	1	3	25.6	25.3	2.66	2	9	11	20	36	6	9	0	NIL
	12.30	00	0	20		Slept 10 mins. (Stage II)															NIL
	17.45	0	0	10		Slept 18 mins. (Stage II)															NIL
SUBJECT M.6	(AET 28)																				
1	22.55	0	0	10	112	487	447	3	30	22.8	14.4	6.50	0	0	6	4	5	47	0	2	NIL
2	23.15	0	0	10	72	484	472	1	6	23.9	23.0	5.63	0	11	5	6	19	27	15	30	NIL
	12.35	0	0	Drowsy only																	NIL
	12.30	0	0	10		Slept 20 mins. (Stage II + III)															NIL
SUBJECT M.7	(AET 32)																				
1	22.55	0	0	21	81	487	391	5	75	14.2	19.6	3.33	0	18	0	26	3	29	0	--	NIL
2	23.00	0	0	51	60	484	432	1	1	10.1	25.6	4.00	0	16	13	0	35	14	32	0	NIL
	12.25	0	0	5		Slept 20 mins. (Stage II)															NIL
	15.30	0	0	10		Slept 16 mins. (Stage II)															NIL

APPENDIX II. SECTION E. IDIOPATHIC HYPERSOMNIA

TABLE I

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (Mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT F.1																					
1	23.33	0	0	26	60	481	449	1	6	21.4	23.5	1.00	0	18	16	0	24	22	21	0	NIL
2	23.10	0	0	30	90	480	440	2	10	20.6	24.3	2.66	0	0	28	26	0	32	11	10	NIL
3	23.16	0	0	20	61	844	743	24	83	17.7	24.3	5.33	0	22	11	24	21	0	16	11	NIL
													21	28	21	0					
4	23.11	0	0	15	160	546	512	6	19	25.2	26.8	3.66	0	0	5	36	21	20	18	10	NIL
5	23.10	0	0	25	120	470	445	0	0	22.6	24.7	3.00	0	0	35	0	17	27	10	21	NIL
6	23.01	0	0	24	66	482	457	1	1	25.1	19.9	2.00	0	28	0	16	20	0	17	10	T5G
	12.30	0	0	5	Slept (Stage II + III) for 25 mins.																NIL
	12.36	0	0	3	Slept 21 mins. (Stage II)																NIL
	19.30	0	0	4	Slept 00 mins. Woke spontaneously																NIL
SUBJECT F.2																					
1	22.30	0	0	2	126	510	500	2	8	15.8	20.6	2.00	0	0	16	28	14	11	21	13	NIL
2	22.40	0	0	5	120	500	495	1	5	16.2	18.4	2.66	0	0	21	18	22	0	16	14	NIL
3	22.36	0	0	7	114	505	490	2	8	14.6	19.4	3.00	0	0	30	0	17	21	11	16	T5G
4	22.15	0	0	10	90	720	590	18	120	13.8	24.6	6.66	0	20	11	0	18	19	21	0	NIL
													16	8	21	11					
	12.15	0	0	Drowsy only																	0
	12.30	0	0	Drowsy only																	0

TABLE II

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT F.3																					
1	22.30	0	0	25	120	510	474	3	11	20.3	19.6	4.83	0	0	16	21	11	14	21	10	NIL
2	22.40	0	0	30	86	505	472	1	3	18.6	23.7	3.00	0	4	16	21	30	8	29	4	NIL
3	22.45	0	0	16	80	499	483	0	0	21.8	26.3	2.00	0	24	0	28	18	16	29	10	NIL
4	22.36	0	0	20	64	506	479	1	7	19.6	23.6	3.66	0	31	0	24	11	17	21	9	T5G
5	22.10	0	0	15	70	720	655	14	50	14.8	23.5	6.00	0	28	10	15	8	21	0	27	NIL
	12.26	0	0	Drowsy only																	NIL
	12.34	0	0	10		Slept 20 mins (Stage II)															NIL
	19.30	0	0	11		Slept 50 mins (Stage II + III)															NIL
SUBJECT F.4																					
1	22.00	0	0	5	52	540	526	2	9	36.8	22.6	1.66	8	26	5	16	21	13	21	9	NIL
2	22.00	0	0	6	48	540	499	4	35	32.9	25.7	3.66	12	16	21	5	11	26	22	15	NIL
3	22.00	0	0	10	58	540	506	3	24	35.1	29.6	2.66	2	27	29	11	16	23	25	17	NIL
	12.30	0	0	4	Stage II sleep for 17 mins.																NIL
	12.38	0	0	6	Stage II + III for 25 mins.																NIL
	19.30	0	0	6	52			REM sleep for 20 mins.													NIL
SUBJECT F.5																					
1	22.50	0	0	6	147	490	482	1	2	20.7	19.3	1.66	0	0	12	10	14	26	8	23	NIL
2	22.46	0	0	26	38	494	416	18	52	11.6	34.4	4.66	22	12	26	19	16	25	18	10	NIL
3	22.45	0	0	36	72	495	457	1	2	21.9	26.0	2.66	0	27	11	14	31	0	17	19	NIL
4	22.40	0	0	22	68	500	476	1	2	22.6	25.8	2.00	0	36	0	28	11	42	0	6	NIL
	12.30	0	0	Drowsy only																	NIL
	19.30	0	0	20		Slept 20 mins. (Stage II)															NIL

TABLE III

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% +	IV%	Rem%	Shifts/ Hour	REM (Mins.) 1 (9)	2 (10)	3 (11)	4 (12)	5	6	7	8	Treatment
SUBJECT F. 6																						
1	22.15	0	0	0	210	585	580	1	5	30.6		13.1	1.00	0	0	0	20	16	8	11	21	NIL
2	22.40	0	0	25	56	500	472	1	3	26.8		22.0	2.33	4	11	23	7	22	9	11	17	NIL
	12.28	0	0	2	Slept 40 mins. (Stage II and III)																	NIL
	12.30	0	0	Drowsy only																		NIL
SUBJECT M. 1																						
1	23.44	0	0	55	107	474	369	8	51	23.4		19.5	4.00	0	0	12	0	17	0	21	22	NIL
2	23.10	0	0	40	120	470	390	3	40	20.6		17.2	3.66	0	0	10	5	16	0	18	18	NIL
3	23.15	0	0	36	109	465	385	4	44	18.8		22.9	4.00	0	0	21	0	26	13	28	0	NIL
4	22.58	0	0	32	92	720	514	21	174	17.5		30.6	7.33	0	0	10	9	27	21	11	0	NIL
														27	8	26	14					
5	22.50	0	0	50	120	490	430	2	10	20.6		17.2	3.00	0	0	11	17	8	21	0	17	T5G
	12.42	0	0	Drowsy only																		NIL
	12.36	0	0	10	Broken sleep. Stages II + III No. REM sleep																	NIL
	17.45	0	0	Drowsy only																		NIL
	19.30	0	0	20	Slept 65 mins. Stage II + III only																	NIL
SUBJECT M. 2																						
1	23.00	0	0	4	69	480	474	1	2	14.8		16.5	2.66	0	12	16	21	0	18	0	7	NIL
2	22.45	0	0	5	62	495	490	0	0	12.6		26.3	1.66	0	22	19	14	26	0	32	16	NIL
3	22.15	0	0	10	76	720	650	5	60	11.4		28.0	5.66	0	25	16	21	0	31	0	42	NIL
														0	11	26	10					
4	22.50	0	0	6	64	490	481	1	3	12.8		24.1	2.33	0	31	0	26	17	8	0	34	T5G
	12.30	0	0	5	12 min Stage II sleep																	NIL
	12.25	0	0	8	Stage II sleep for 36 mins.																	NIL
	17.30	0	0	6	Slept 40 mins. (Stage II + III)																	NIL

TABLE IV

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
													(9)	(10)	(11)	(12)					
SUBJECT M.3																					
1	22.40	0	0	12	96	503	460	4	31	33.4	31.7	3.33	0	16	26	13	12	10	54	15	NIL
2	22.50	0	0	24	147	482	458	0	0	21.9	18.8	5.83	0	0	18	11	15	16	1	25	NIL
3	22.56	0	0	60	56	499	431	4	8	15.6	26.7	4.33	0	8	14	25	6	22	5	35	NIL
4	22.59	0	0	16	59	486	470	0	0	27.4	24.3	3.83	1	10	15	8	20	0	25	33	T5G
	12.30	0	0	5		Stage II 5 mins.															NIL
	12.46	0	0	Drowsy only																	NIL
SUBJECT M.4																					
1	22.50	0	0	8	96	499	432	6	59	27.1	28.9	1.16	0	24	10	21	0	36	21	14	NIL
2	22.46	0	0	16	90	494	446	4	32	22.1	22.0	2.0	0	21	0	36	11	14	0	16	NIL
3	22.45	0	0	6	84	484	476	1	2	21.6	27.1	2.66	0	26	11	0	35	12	11	29	T5G
4	22.15	0	0	10	98	720	658	14	52	17.0	27.7	6.00	0	32	0	17	18	26	12	8	NIL
	12.32	0	0	15	Slept momentarily (Few sleep spindles)																NIL
	12.40	0	0	Drowsy only																	NIL
	17.30	0	0	10	Slept 18 mins. (Stage II)																NIL
	19.30	0	0	15	Slept 45 mins. (Stage II + III)																NIL
SUBJECT M. 5																					
1	22.45	0	0	6	58	495	480	3	9	28.6	25.0	2.00	0	26	14	18	11	0	21	30	NIL
2	22.50	0	0	10	74	490	472	2	8	26.4	23.7	2.00	0	31	6	25	0	11	17	22	NIL
3	22.14	0	0	16	62	720	683	6	21	25.4	28.7	4.66	0	36	0	31	24	0	13	26	NIL
													21	0	17	29					
4	22.40	0	0	6	70	500	482	3	12	24.6	25.7	3.00	0	28	11	26	10	30	15	4	T5G
	12.32	0	0	Drowsy only																	NIL
	12.46	0	0	16	Stage II 10 mins.																NIL
	17.40	0	0	20	Slept 36 mins. (Stage II)																NIL
	19.40	0	0	11	Slept 42 mins. (Stage II)																NIL

TABLE V

Night	Start	D(Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.6													(9)	(10)	(11)	(12)					
1	22.40	0	0	16	70	500	481	1	3	23.6	23.7	2.00	0	26	0	34	16	11	21	6	NIL
2	22.56	0	0	10	64	484	447	3	27	28.4	24.2	1.33	0	16	22	6	26	8	31	0	NIL
3	22.16	0	0	8	56	715	699	4	8	26.4	20.6	6.33	0	31	0	27	6	11	21	10	NIL
													0	17	21	0					
	12.26	0	0	10	Slept 30 mins. (Stage II + III)																NIL
	12.36	0	0	Drowsy only																	NIL
	17.36	0	0	15		Slept 6 mins. (Stage II)															NIL
	19.32	0	0	6		Slept 48 mins. (Stage II)															NIL
SUBJECT M.7																					
1	22.45	0	0	14	144	495	470	2	11	12.8	17.4	4.66	0	0	10	21	0	11	26	14	NIL
2	22.40	0	0	6	126	500	494	0	0	14.8	21.1	2.00	0	0	28	27	11	14	16	8	NIL
3	22.50	0	0	10	120	490	479	1	1	13.6	22.8	1.66	0	0	26	21	14	18	21	9	NIL
	12.35	0	0	Drowsy only																	NIL
	19.40	0	0	Drowsy. No sleep																	NIL

APPENDIX II. SECTION F. KLEINE LEVIN SYNDROME

Night	Onset	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
													(9)	(10)	(11)	(12)					
SUBJECT F.1																					
1	22.58	0	0	10	78	512	472	6	30	24.9	18.6	4.33	0	21	0	16	13	0	26	12	NIL
2	23.10	0	0	6	80	500	483	3	11	26.8	23.2	2.00	0	32	0	26	11	0	29	14	NIL
3	22.50	0	0	12	96	510	491	1	7	25.2	22.4	3.00	0	20	11	21	16	5	31	6	NIL
4	22.56	0	0	8	72	514	496	2	10	23.8	28.2	3.66	0	19	26	12	0	31	20	32	T5G
	12.32	0	0	No sleep in 30 mins.																	NIL
	13.00	0	0	8		Slept 10 mins. (Stage II)															NIL
	17.36	0	0	Drowsy only																	NIL
	19.32	0	0	10		Slept 20 mins. (Stage II)															
SUBJECT M.1																					
1	22.40	0	0	14	92	514	497	1	3	22.6	16.3	2.66	0	21	0	22	13	0	16	9	NIL
2	22.52	0	0	6	84	716	672	8	38	21.2	25.0	4.66	0	26	10	15	0	16	31	25	NIL
													0	16	18	11					
3	22.50	0	0	11	80	510	486	3	13	23.7	18.7	3.00	0	18	14	6	10	29	0	14	NIL
4	22.59	0	0	8	64	483	470	2	5	22.9	20.4	3.66	0	27	11	21	0	17	14	6	T5G
	12.30	0	0	No sleep in 30 mins.																	NIL
	12.36	0	0	5		Slept 5 mins. (Stage II)															NIL
	19.36	0	0	11		Slept 36 mins. (Stage II + III)															NIL
	19.41	0	0	24		Slept 26 mins. (Stage II)															NIL
SUBJECT M.2																					
1	22.46	0	0	42	116	524	461	4	21	19.6	20.0	4.66	0	4	21	16	0	11	26	14	NIL
2	22.52	0	0	13	81	516	490	2	13	21.4	21.0	2.00	0	26	11	0	17	31	0	16	NIL
3	22.51	0	0	8	61	511	493	1	10	24.6	20.3	1.33	0	30	14	0	6	18	21	11	NIL
4	22.45	0	0	16	72	525	503	1	6	23.0	19.5	2.00	0	36	0	14	11	21	0	16	T5G
	12.26	0	0	10		Slept 16 mins. (Stage II)															NIL
	19.30	0	0	5		Slept 45 mins. (Down to Stage IV)															NIL

APPENDIX II, SECTION G. PICKWICKIAN SYNDROME

Night	Start	D (Rem)	SOREM	d	D	TTB	TST	A	TA	III% + IV%	Rem%	Shifts/ Hour	REM (mins.) 1	2	3	4	5	6	7	8	Treatment
SUBJECT M.1																					
1	22.48	0	0	42	133	489	319	25	129	NIL	10.3	11.1	0	0	3	0	9	5	6	10	NIL
2	22.15	0	0	45	105	499	366	14	27	NIL	7.5	10.1	0	11	0	3	0	0	12	0	NIL
3	22.45	0	0	8	146	480	405	5	68	NIL	9.7	9.33	0	0	25	2	0	3	2	12	NIL
4	22.43	0	0	26	147	528	432	11	70	NIL	9.0	9.0	0	0	4	5	1	2	12	24	NIL
5	23.13	0	0	24	179	479	339	23	116	3.3	6.9	9.66	0	0	18	0	0	8	0	0	NIL
6	23.24	0	0	17		498	256	12	225	19.1	0	4.33	0	0	0	0	0	0	0	0	Salicyclic Ac
	12.32	0	0	Drowsy only			Cycles of Stage I			Arousal 20-40 secs											NIL
	17.30	0	0	Drowsy only			Cycles of Stage I			Arousal 20-30 secs											NIL
	19.30	0	0	18	Stage I with very poor sleep					(10 mins)											NIL
SUBJECT M.2																					
1	22.46	0	0	38	197	482	386	6	58	NIL	12.4	11.66	0	0	0	3	16	0	24	5	NIL
2	23.14	0	0	28	66	457	422	3	7	10.4	17.4	7.0	2	16	0	1	29	16	8	-	NIL
3	22.52	0	0	22	239	458	404	4	32	NIL	11.6	29.3	0	0	0	1	23	0	14	9	NIL
	12.40	0	0	6	Cycle of Stage I + II			40-50 secs													NIL
	19.50	0	0	14	Cycles of Stage I + II			30-50 secs													NIL

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SUMMARY

A total of fifty-four patients presenting with complaints which included sleep attacks or excessive sleep, were referred from local neurological and psychiatric clinics and hospitals during a five year period, 1965-70.

A clinical diagnosis of Idiopathic narcolepsy was made in thirty cases (14 female, 16 male). Symptomatic narcolepsy (2 female, 4 male). Pickwickian syndrome (2 male), Kleine Levin (1 female, 2 male) and Idiopathic hypersomnia (6 female, 7 male).

The basic concepts in the development of the hypersomnia syndromes was described.

Clinical information was collected from each subject at initial interview and physical investigations which included a full blood count, protein bound iodine estimate, lumbar puncture and plasma glucose at the time of a diurnal sleep episode were carried out.

Polygraphic recordings of electroencephalogram, electro-occulogram, submental percutaneous muscle tone and heart rate, were made of overnight sleep on several occasions at intervals. Recordings of diurnal sleep episodes were made at several times of day.

Serial samples of venous blood were obtained from two hypersomnia patients and analysed for serum glucose level. Serial arterial blood samples during sleep were taken from both Pickwickian patients and overall changes in blood gases were recorded.

Sleep records were scored according to internationally agreed criteria. Cycles of slow wave (orthodox) sleep with alternating Rapid Eye Movements sleep (REM or paradoxical sleep) were noted in all records.

Analysis of clinical data was compared with relevant clinical studies and the patient group was found to be compatible with previously published patient series.

A male preponderance was noted throughout the clinical groups, and an onset in adolescence or early adult life was usual. Most patients show their symptoms as static or subject to fluctuations. Thyroid disorder, hypoglycaemia and cerebral diseases did not contribute to the symptoms, although there was evidence of cerebral pathology in the symptomatic narcoleptic group. Obesity and appetite was frequently present in all patient groups and psychological symptoms were also frequently present.

Polygraphic studies showed that narcoleptics with symptoms of sleep paralysis, Cataplexy or hypnogogic hallucinations suffered from a unique disorder of sleep, not present in a control group of normal subjects. Sleep onset was associated with a REM sleep period (SOREM period) and this precipitous period of REM sleep with attendant change in muscle tone and dream activity was found to account for the narcoleptic symptom tetrad. Both idiopathic and symptomatic narcoleptics showed an increased tendency to slow wave sleep.

Pickwickian patients showed a distinct and significant alteration of sleep and respiration consisting of cycles of apnoea broken by periods of noisy hypernoea. Sleep was grossly interrupted by this process. One patient showed an inability to control levels of blood gases during sleep and was found to be remarkably insensitive to hypoxia whichawhen awake produced dramatic respiratory increase. These patients however differed from the classical description of the Pickwickian syndrome and showed no evidence of resting hypercapnia, polycythaemia and circulatory disorder.

The sleep of the remaining hypersomnia patients was not abnormal although excessive. No significant sleep disorder was found in the clinical Kleine-Levin group of patients. Cases of drug abuse and patients who had voluntary altered sleep habits were excluded from this group which significantly altered the constituent of the group. The typical hypersomnia patient is a young adult male who developed excessive sleep during adolescence. Psychological problems were found in all cases, and considered to be the prime aetiological factor.

The validation of the clinical syndromes in relation to clinical and polygraphic data was discussed in relation to recent published studies of similar patients.

It was suggested that each hypersomnia syndrome was fundamentally bipolar. At one end of the continuum patients with physical or brain disorders formed a nuclear group whilst at the other patients with psychiatric disorder formed a similar but contrasting group.

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A clinical diagnosis of Idiopathic narcolepsy was made in thirty cases (14 female, 16 male). Symptomatic narcolepsy (2 female, 4 male). Pickwickian syndrome (2 male), Kleine Levin (1 female, 2 male) and Idiopathic hypersomnia (6 female, 7 male).

The basic concepts in the development of the hypersomnia syndromes was described.

Clinical information was collected from each subject at initial interview and physical investigations which included a full blood count, protein bound iodine estimate, lumbar puncture and plasma glucose at the time of a diurnal sleep episode were carried out.

Polygraphic recordings of electroencephalogram, electro-occulogram, submental percutaneous muscle tone and heart rate, were made of overnight sleep on several occasions at intervals. Recordings of diurnal sleep episodes were made at several times of day.

Serial samples of venous blood were obtained from two hypersomnia patients and analysed for serum glucose level. Serial arterial blood samples during sleep were taken from both Pickwickian patients and overall changes in blood gases were recorded.

Sleep records were scored according to internationally agreed criteria. Cycles of slow wave (orthodox) sleep with alternating Rapid Eye Movements sleep (REM or paradoxical sleep) were noted in all records.

Analysis of clinical data was compared with relevant clinical studies and the patient group was found to be compatible with previously published patient series.

A male preponderance was noted throughout the clinical groups, and an onset in adolescence or early adult life was usual. Most patients show their symptoms as static or subject to fluctuations. Thyroid disorder, hypoglycaemia and cerebral diseases did not contribute to the symptoms, although there was evidence of cerebral pathology in the symptomatic narcoleptic group. Obesity and appetite was frequently present in all patient groups and psychological symptoms were also frequently present.

Polygraphic studies showed that narcoleptics with symptoms of sleep paralysis, Cataplexy or hypnogogic hallucinations suffered from a unique disorder of sleep, not present in a control group of normal subjects. Sleep onset was associated with a REM sleep period (SOREM period) and this precipitous period of REM sleep with attendant change in muscle tone and dream activity was found to account for the narcoleptic symptom tetrad. Both idiopathic and symptomatic narcoleptics showed an increased tendency to slow wave sleep.

Pickwickian patients showed a distinct and significant alteration of sleep and respiration consisting of cycles of apnoea broken by periods of noisy hypernoea. Sleep was grossly interrupted by this process. One patient showed an inability to control levels of blood gases during sleep and was found to be remarkably insensitive to hypoxia whichawhen awake produced dramatic respiratory increase. These patients however differed from the classical description of the Pickwickian syndrome and showed no evidence of resting hypercapnia, polycythaemia and circulatory disorder.

The sleep of the remaining hypersomnia patients was not abnormal although excessive. No significant sleep disorder was found in the clinical Kleine-Levin group of patients. Cases of drug abuse and patients who had voluntary altered sleep habits were excluded from this group which significantly altered the constituent of the group. The typical hypersomnia patient is a young adult male who developed excessive sleep during adolescence. Psychological problems were found in all cases, and considered to be the prime aetiological factor.

The validation of the clinical syndromes in relation to clinical and polygraphic data was discussed in relation to recent published studies of similar patients.

It was suggested that each hypersomnia syndrome was fundamentally bipolar. At one end of the continuum patients with physical or brain disorders formed a nuclear group whilst at the other patients with psychiatric disorder formed a similar but contrasting group.